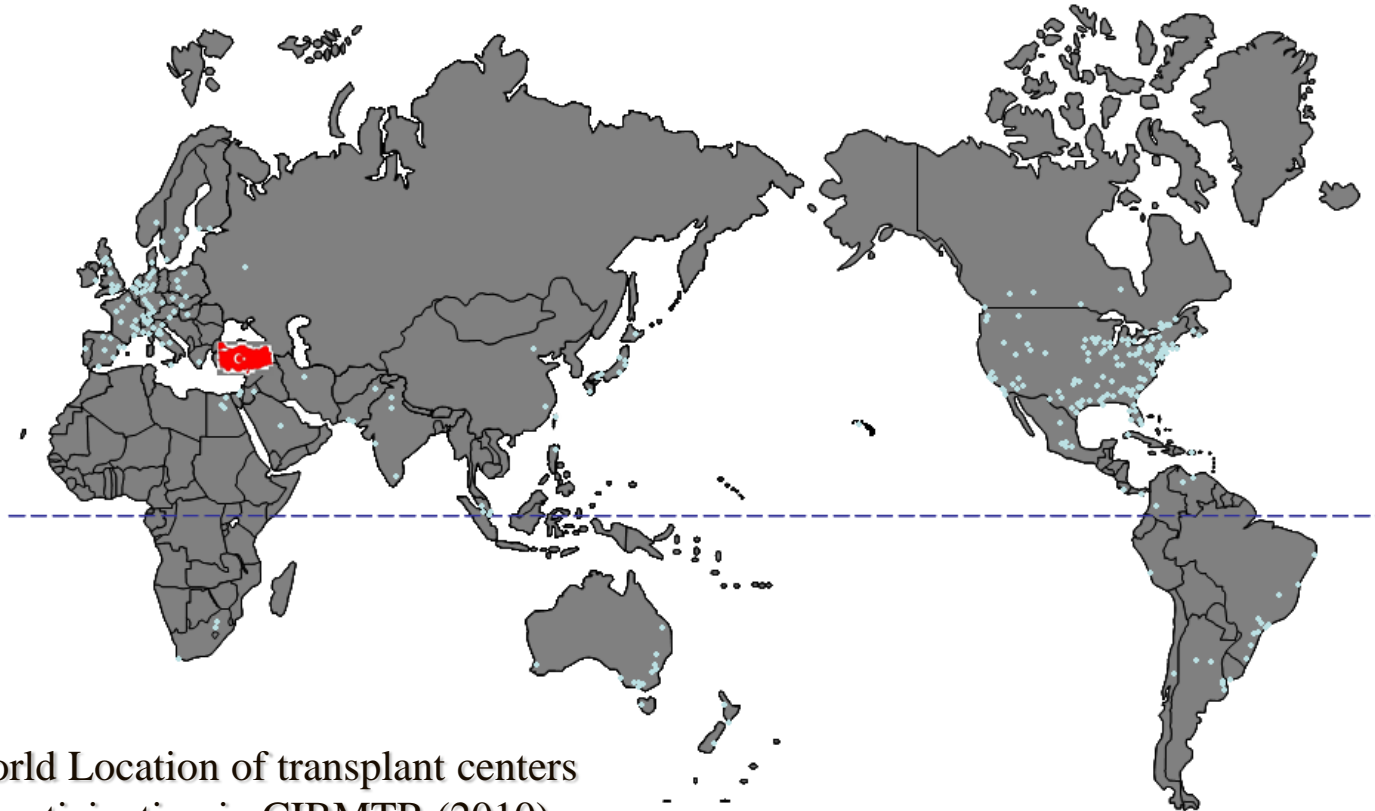


# Hematopoietic Stem Cell Therapies in TURKIYE



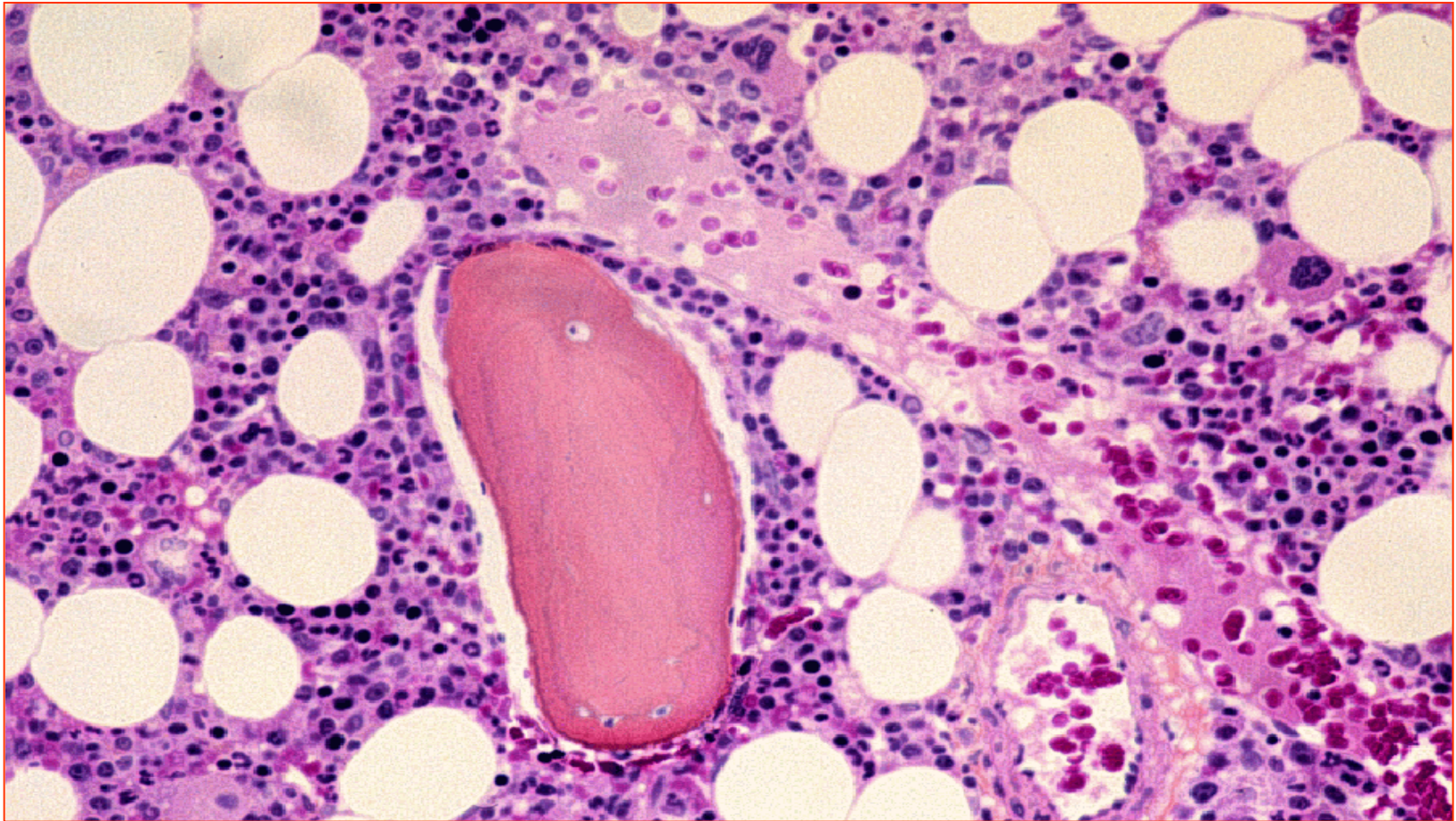
World Location of transplant centers  
participating in CIBMTR (2010)

Mustafa CETIN, M.D.  
Erciyes University Medical Faculty  
Kayseri-TURKIYE

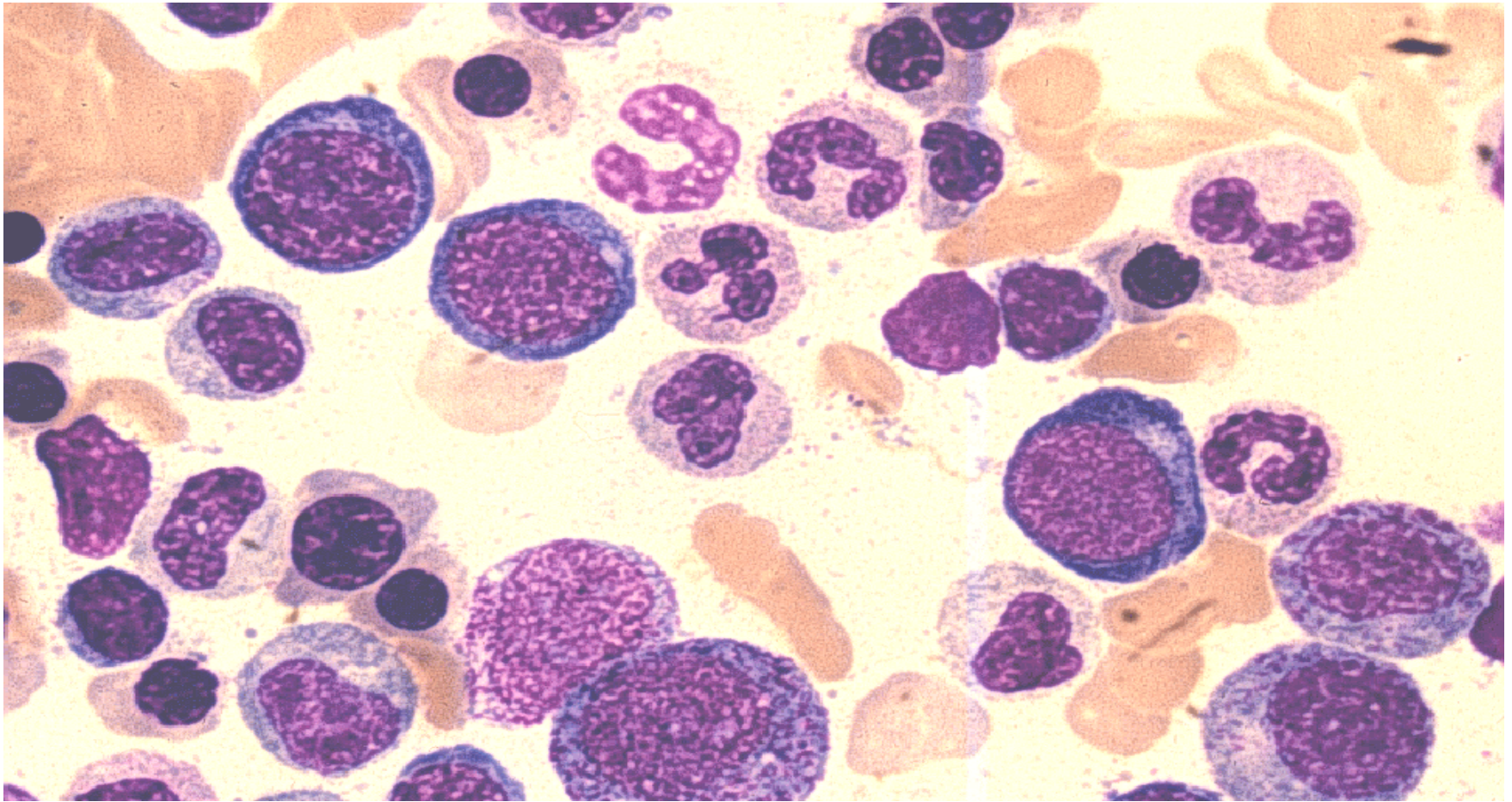
# *Background*

- Bone Marrow Function
- Hematopoietic Stem Cell (Bone Marrow) Transplantation
- Hematopoietic Stem Cell Therapy Results
- Transplantation Activity Survey (Europa & US & World)
- Transplantation Activity Survey (TURKIYE)
- Transplantation Activity Survey (ERCIYES)

# *Bone Marrow: Function*

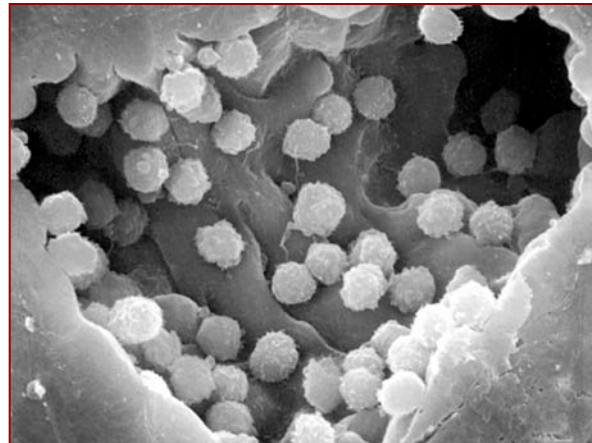
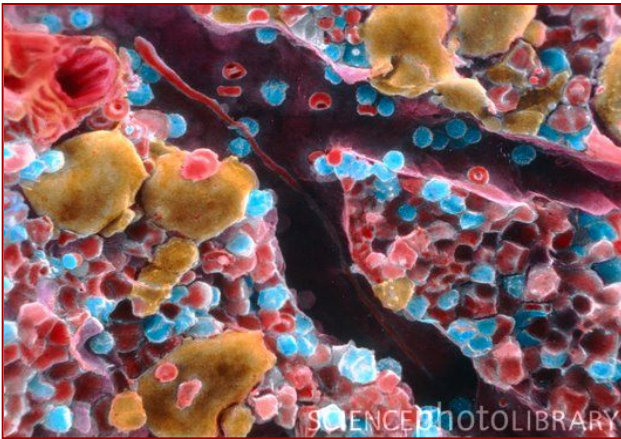


# *Bone Marrow: Function*



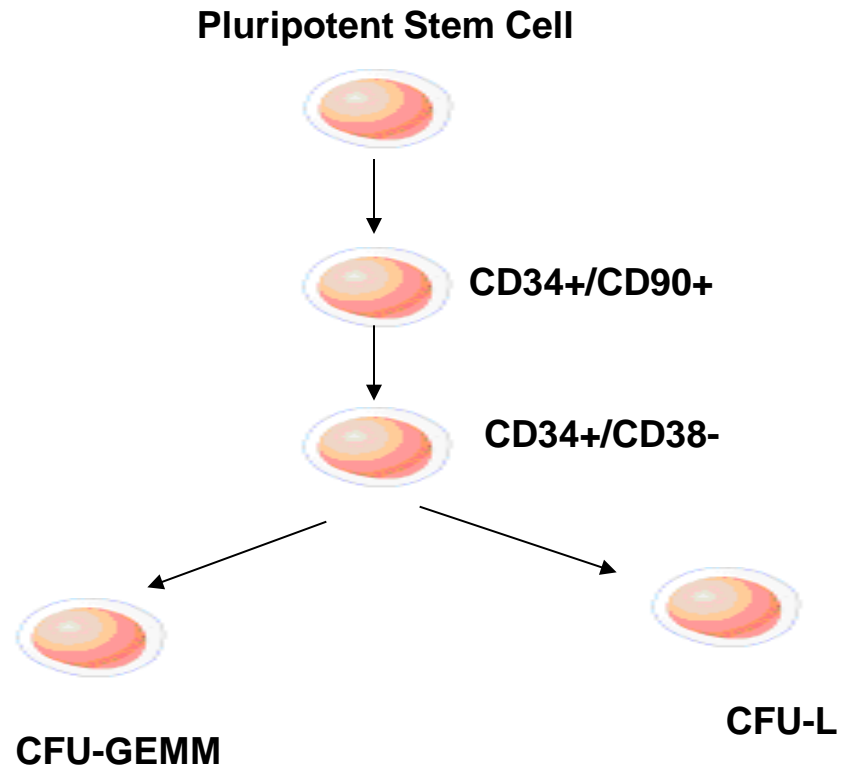
# *Bone Marrow: Function*

- Production of blood cells,
  - 175 billion red cells/day
  - 70 billion granulocytes/day (neutrophils, eosinophils, basophils)
  - 175 billion platelets/day
  - Capable of 5-10 fold increase in production

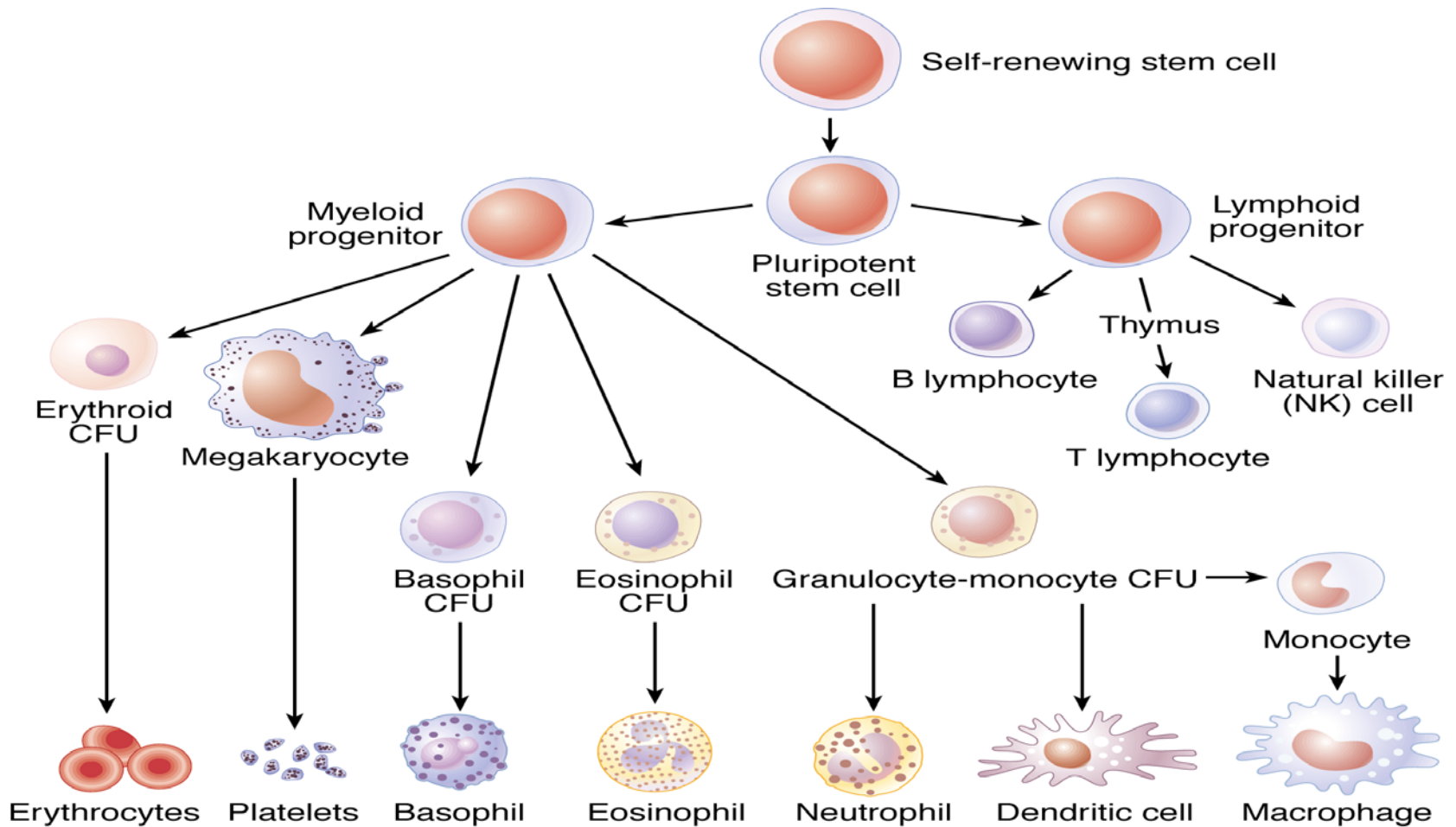


1- 0.1% human  
bone marrow  
cells are early  
hematopoietic  
cell precursors

# *Experimental Model of Early Hematopoiesis*

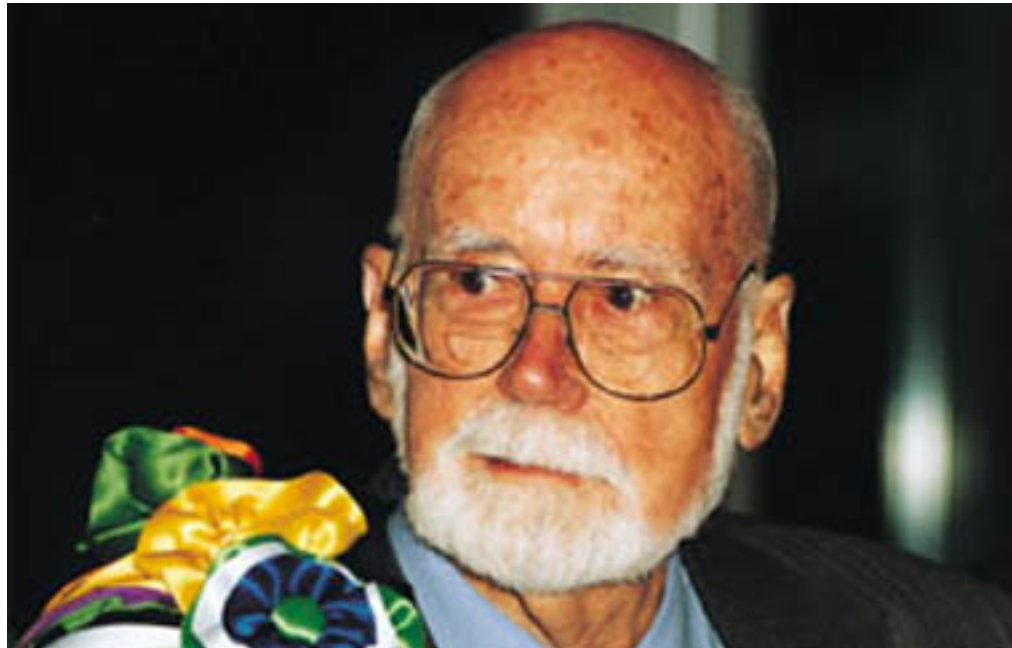


# Bone Marrow hematopoiesis



The Nobel Prize, 1990

E. Donnall Thomas

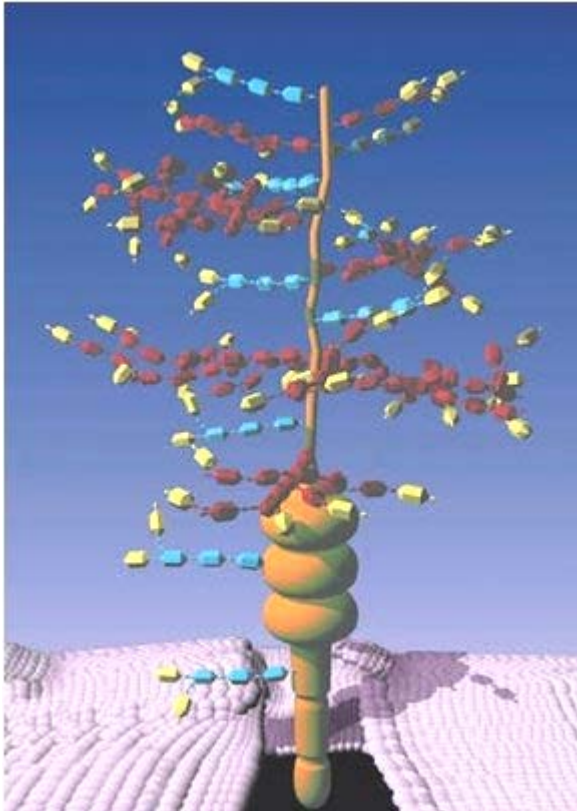


first successful clinical HSCT in treatment of acute leukemias

*Thomas ED, Lochte HL, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N. Engl. J. Med. 1957; 257: 491.*



# What is CD 34 anyway ?



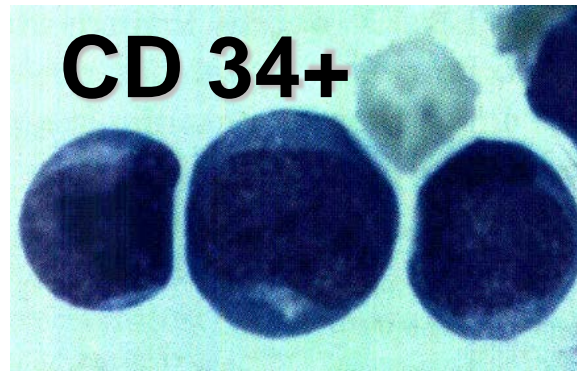
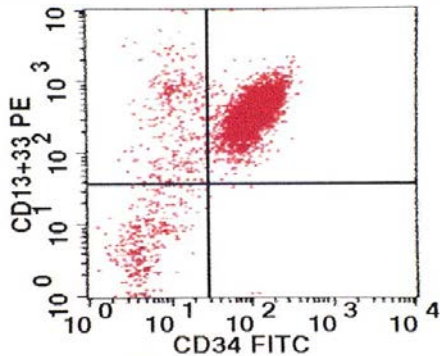
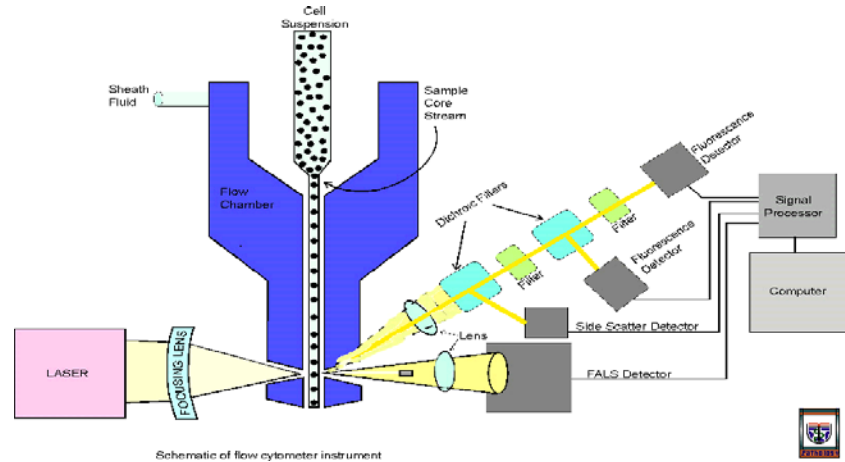
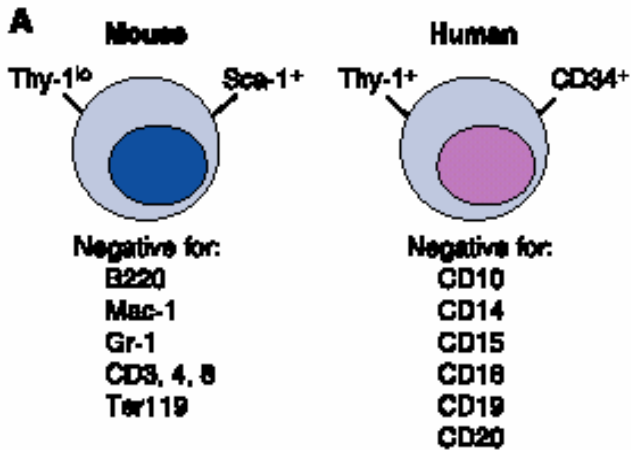
- 105-120 kDa transmembrane Glycoprotein
- Present in early hematopoietic cell precursors
- Present in 0.1% of peripheral mononuclear cells  
1-4% human bone marrow cells

**Probably an adhesion molecule.**



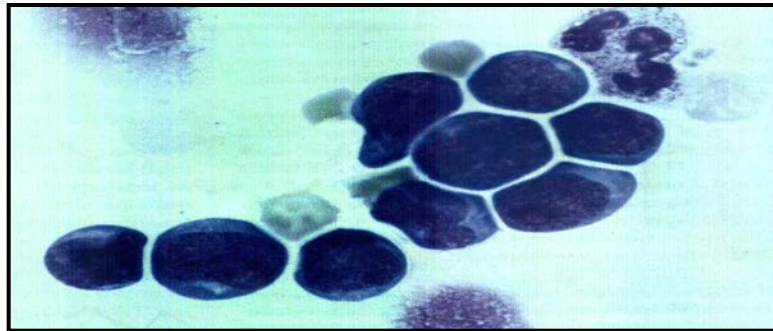
# Hematopoietic stem cell (immunophenotyping)

CD34+, Thy1+, CD38-, HLA-DR-, c-kit+, Lin-, AC133+, CD33-, CD4-, CD8-, CD14-, CD19-,



# *Hematopoietic stem cell harvesting*

**How can we get CD34+  
hematopoietic stem cell ?**



- Bone marrow harvesting
- Peripheral blood harvesting

# *Bone marrow harvesting*

- General anaesthetic
- Marrow aspirated from pelvis  
(+sternum)
- Marrow filtered to remove debris
- Marrow may be administered  
“fresh” or cryo-preserved



# Peripheral blood harvesting

- **Stem cells mobilised –**
  - G-CSF in healthy donors
  - Cyclophosphamide + G-CSF in patients
- **On day 5 (donors), day 10 (patients)**
  - 3 hours session on stem cell collection machine
- **Stem cells given fresh or cryopreserved**

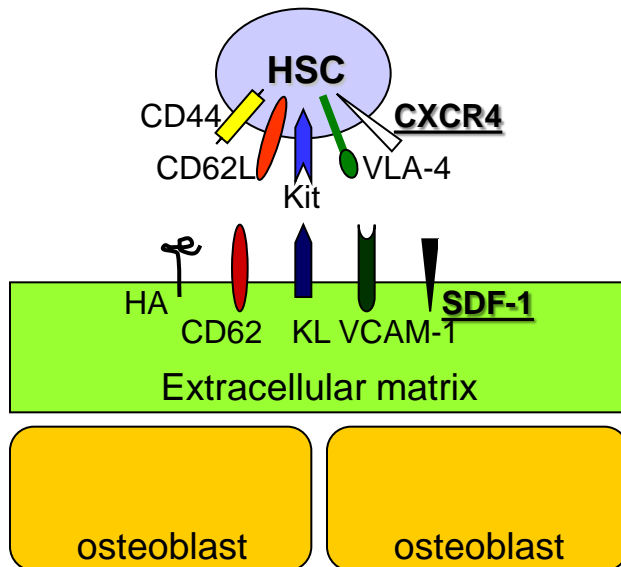


# G-CSF mobilization

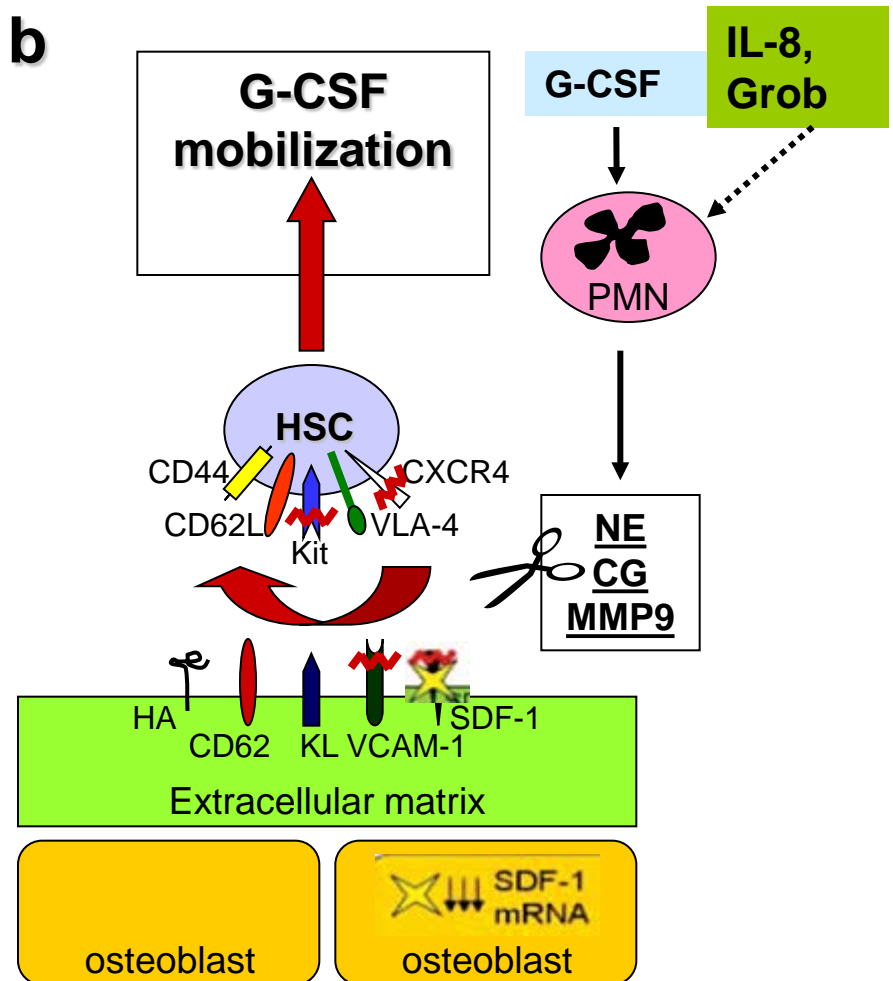
## The role of proteases (NE, CG, and MMP9)

**a**

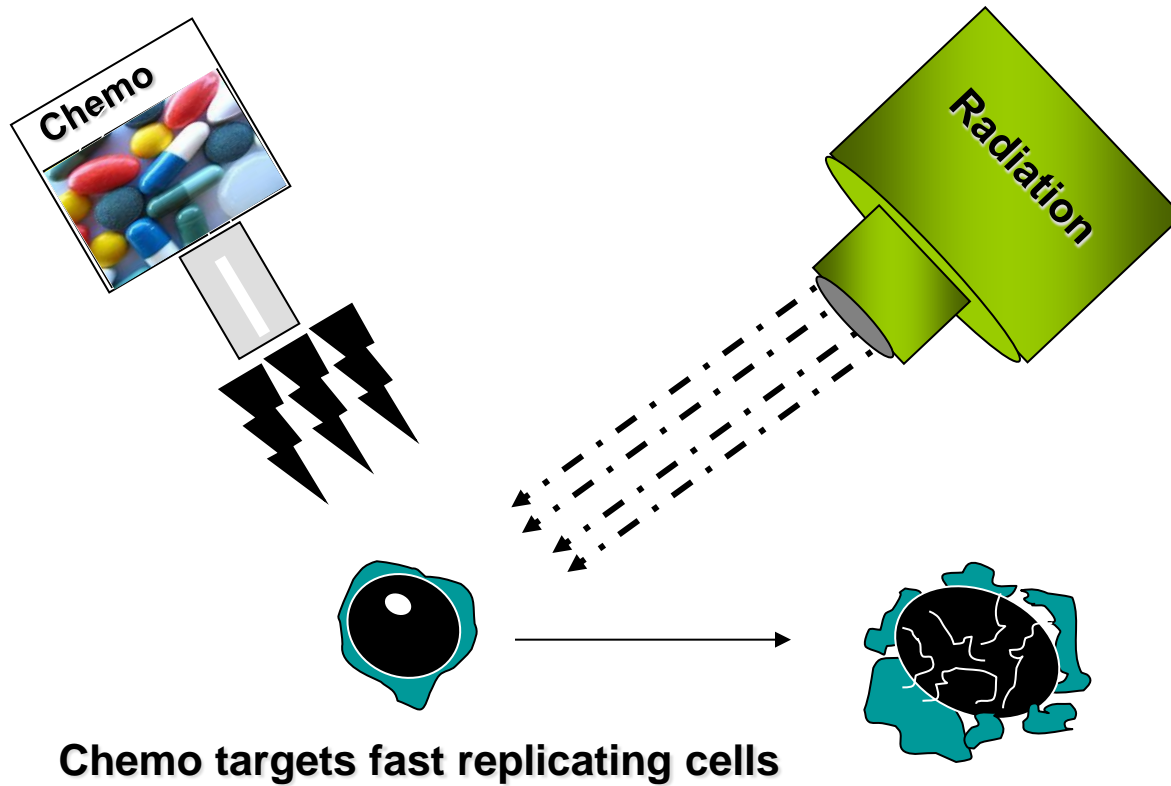
adhesive interactions  
between HSC and BM:  
cell adhesions molecules



**b**

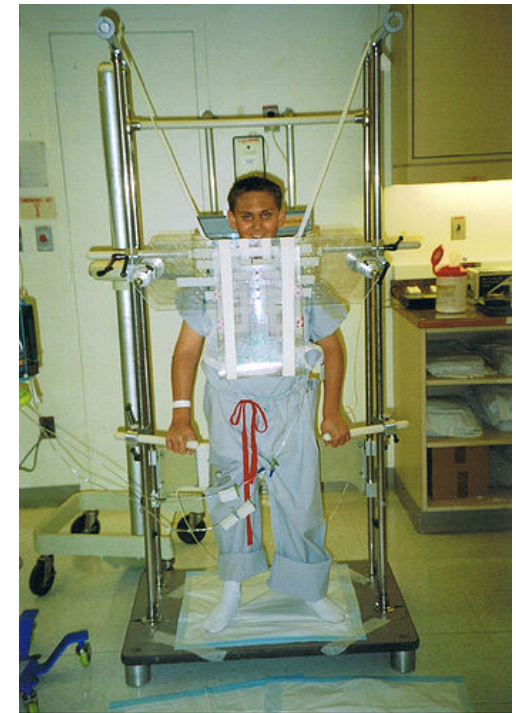
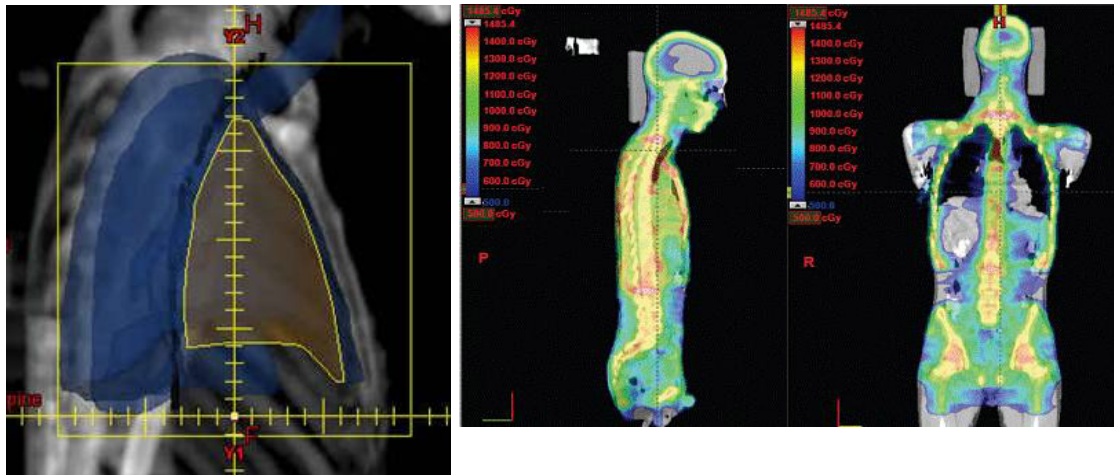


# *Stem Cell Transplant: Effects of Treatment*



# Myelo-ablation

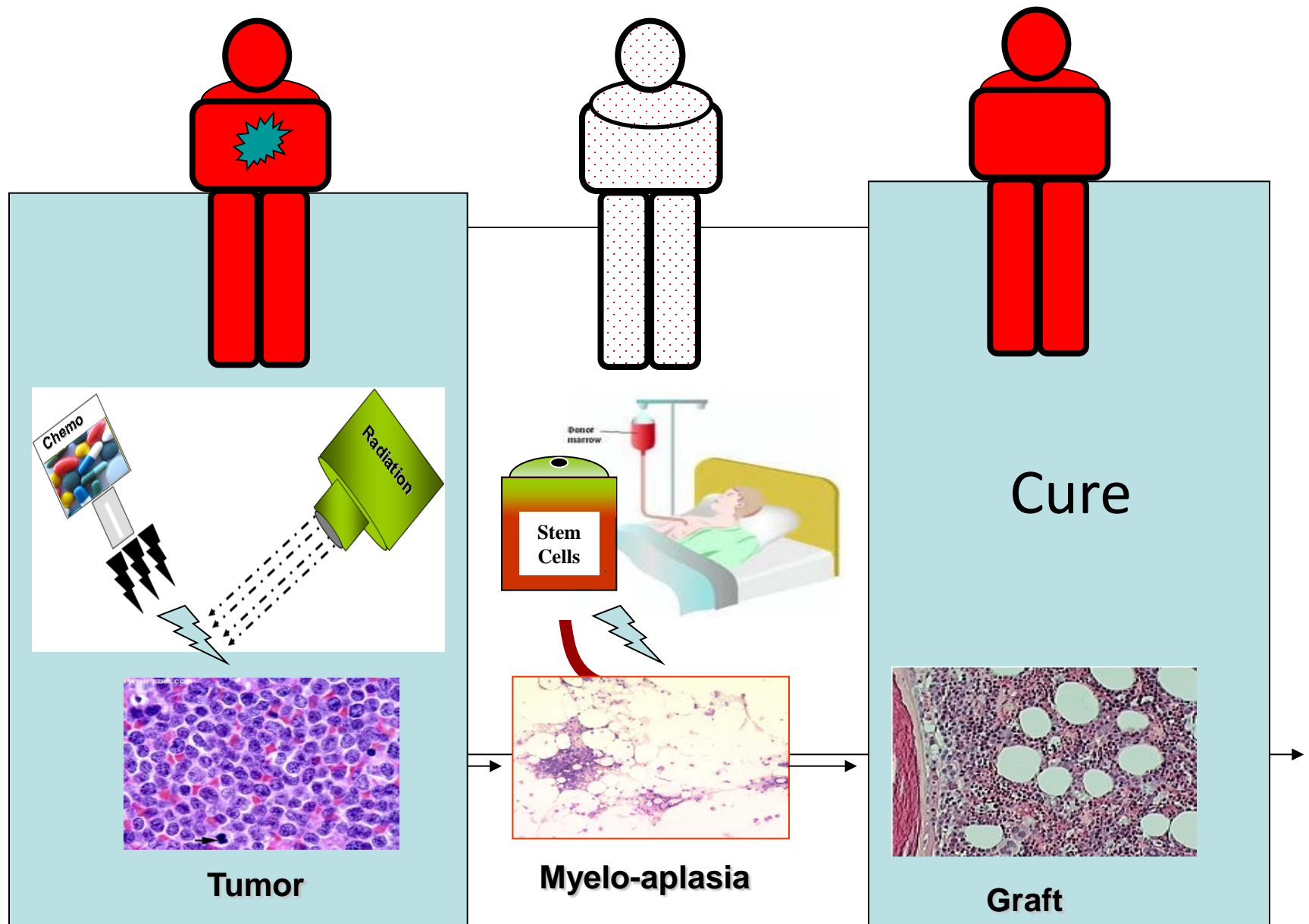
- Total body irradiation 10-12 Gy (fractionated) + cyclophosphamide
- Cyclophosphamide + busulfan



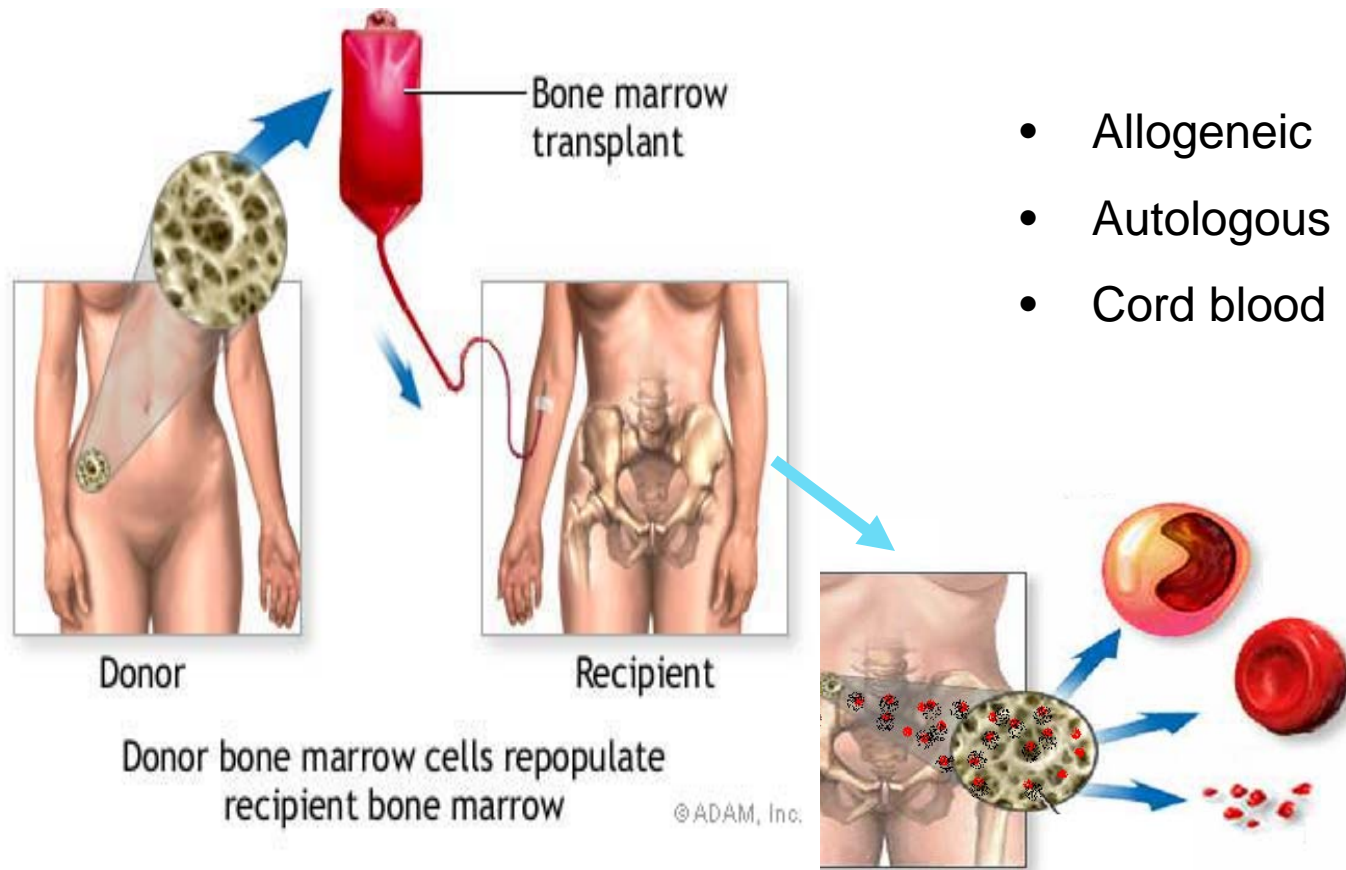
Nb 4.5 Gy fatal in 50% exposed individuals



# Rational of BMT



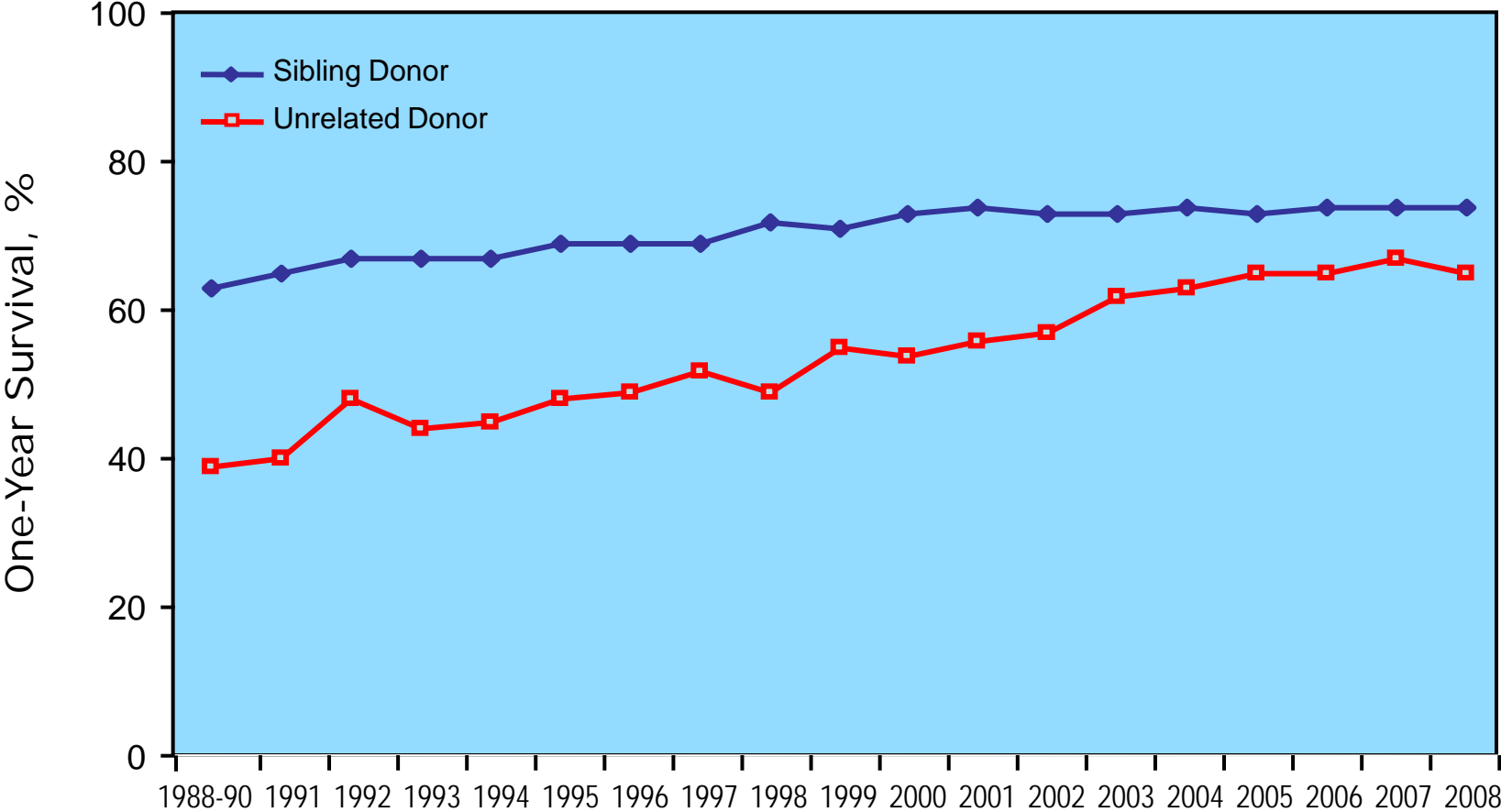
# Types of stem cell for transplantation



# BMT/ PBSC Transplants: Indications

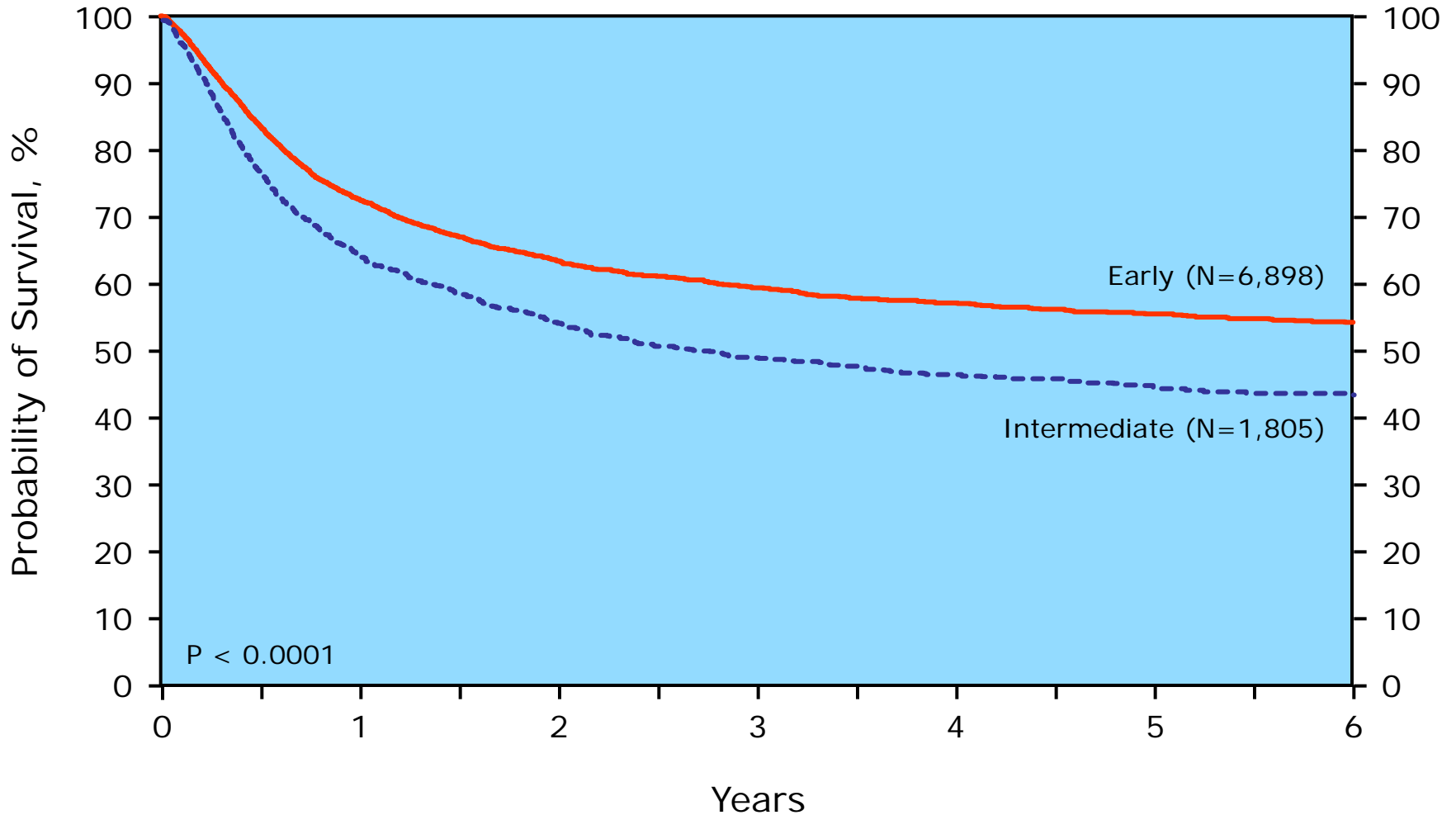
- Leukemias (acute and chronic)
- Lymphomas (Hodgkin's and non-Hodgkin's)
- Multiple myeloma
- Myelodysplastic and myeloproliferative disease
  - (myelofibrosis, polycythemia vera, essential thrombocytosis)
- Aplastic anemia
- Metastatic breast cancer \*
- Some metabolic diseases
- childhood cancers (neuroblastoma, sarcomas, high grade gliomas, Wilm's tumor)
- Congenital immunodeficiencies (CGD, SCID, Wiskott-Aldrich)
- Rheumatologic/autoimmune diseases (RA, jRA, Lupus, AIHA)
- Hemoglobinopathies
- Metabolic diseases (osteopetrosis, Hurler's, adrenaleukodystrophy)

# Trends of transplant survival RATE & succes , age <50 years, by year of transplant and graft source, 1988-2008

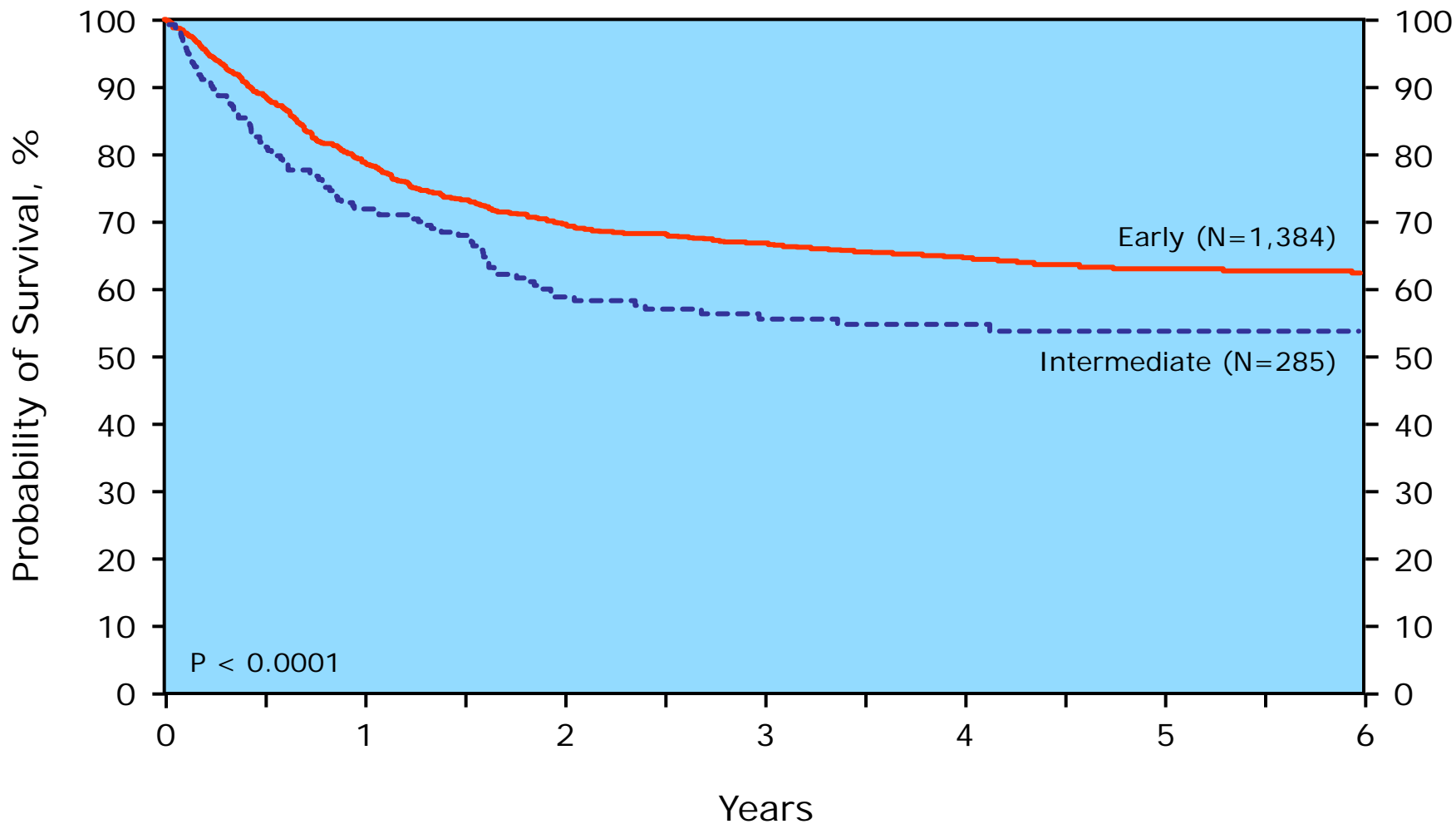


# Probability of survival for AML

HLA-matched sibling donor transplant, by disease status, 1998-2008

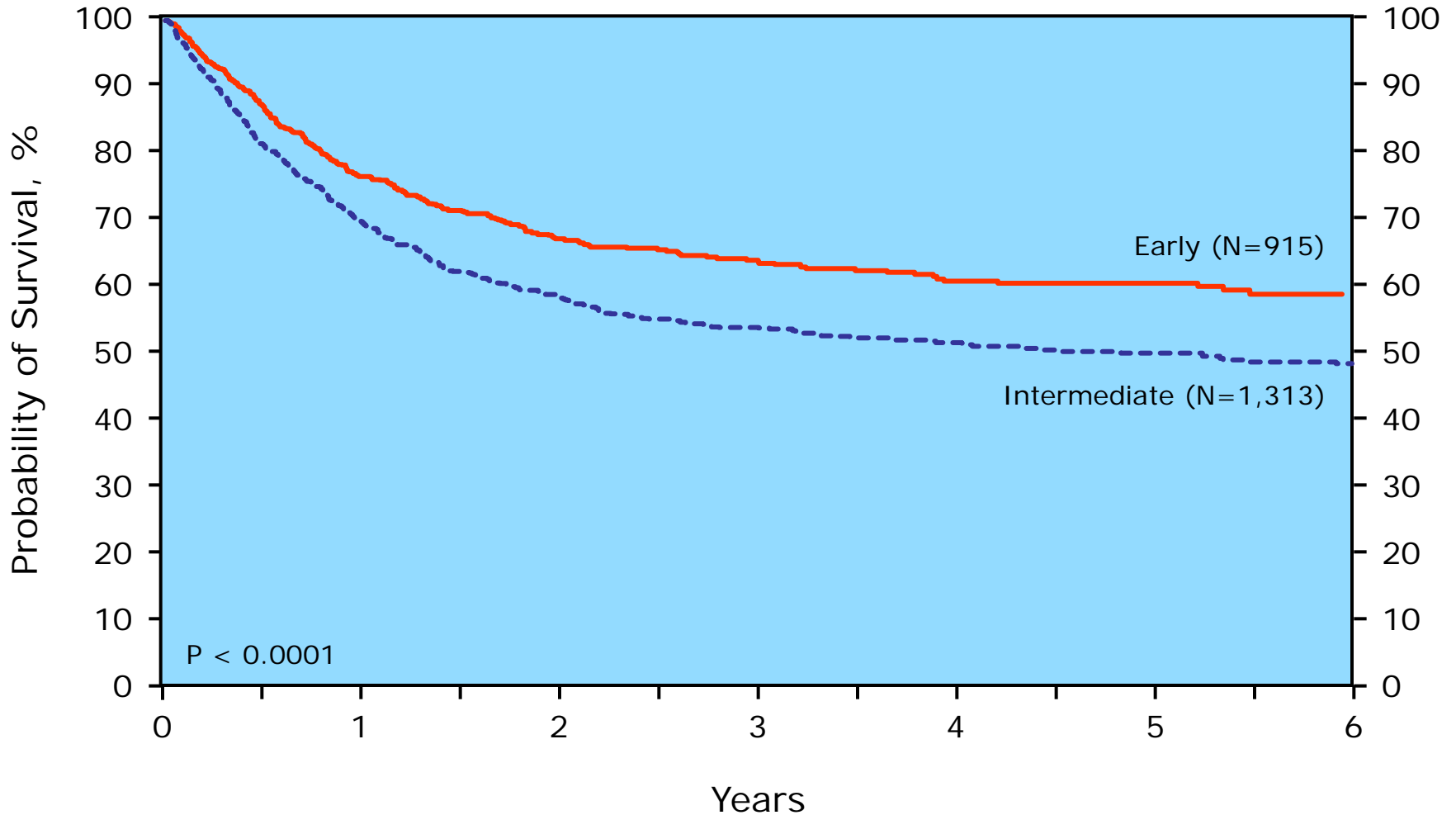


# Probability of survival for AML , HLA-matched sibling donor transplant, age <20 years, by disease status, 1998-2008



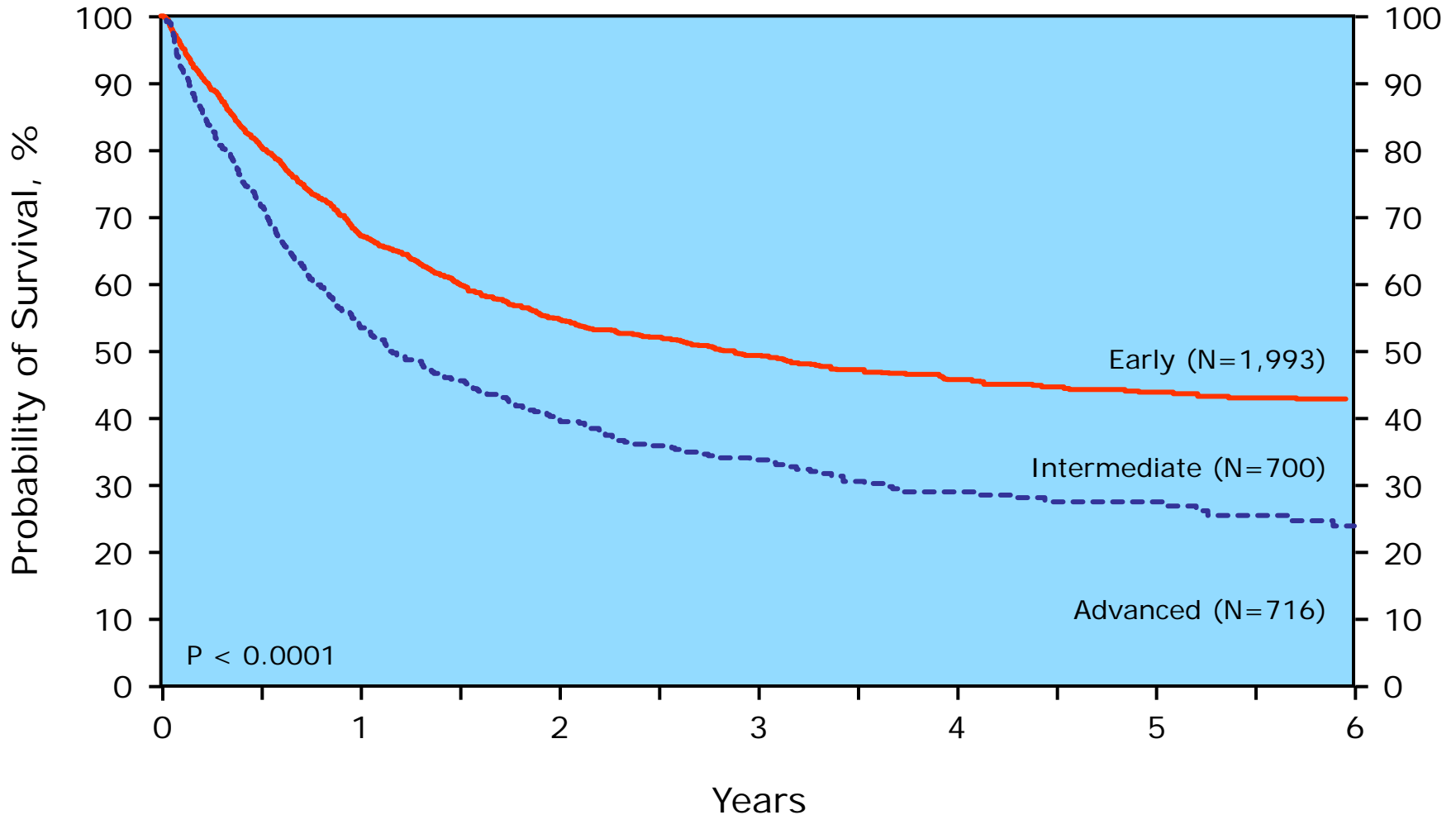
# Probability of survival for ALL

HLA-matched sibling donor transplant, age <20 years, by disease status, 1998-2008



# Probability of survival for ALL

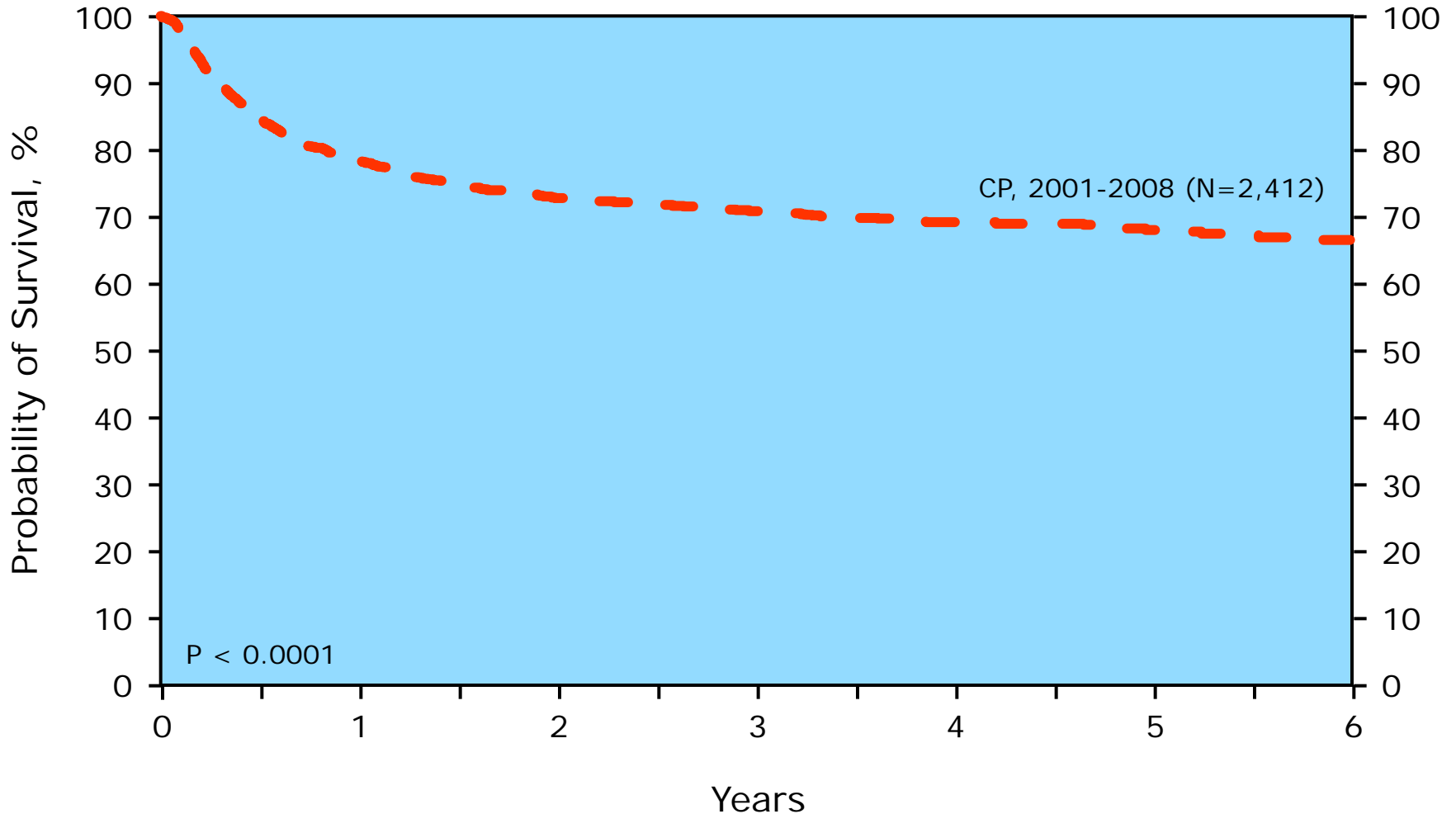
HLA-match sibling donor transplant, age  $\geq 20$  years, by disease status, 98-2008



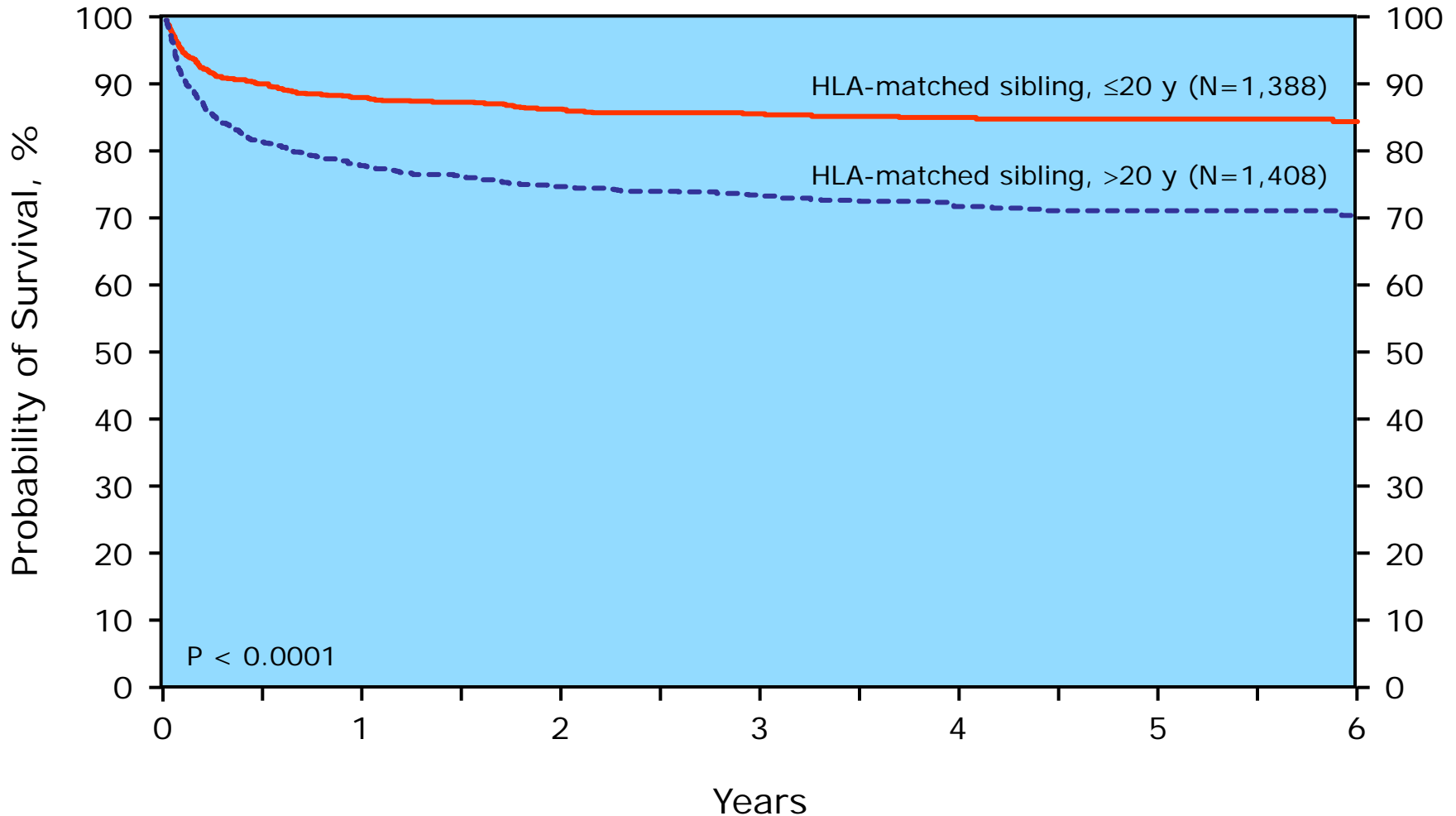


# Probability of survival for CML

HLA-match sibling donor transplant, by disease status and transplant year, 98-2008

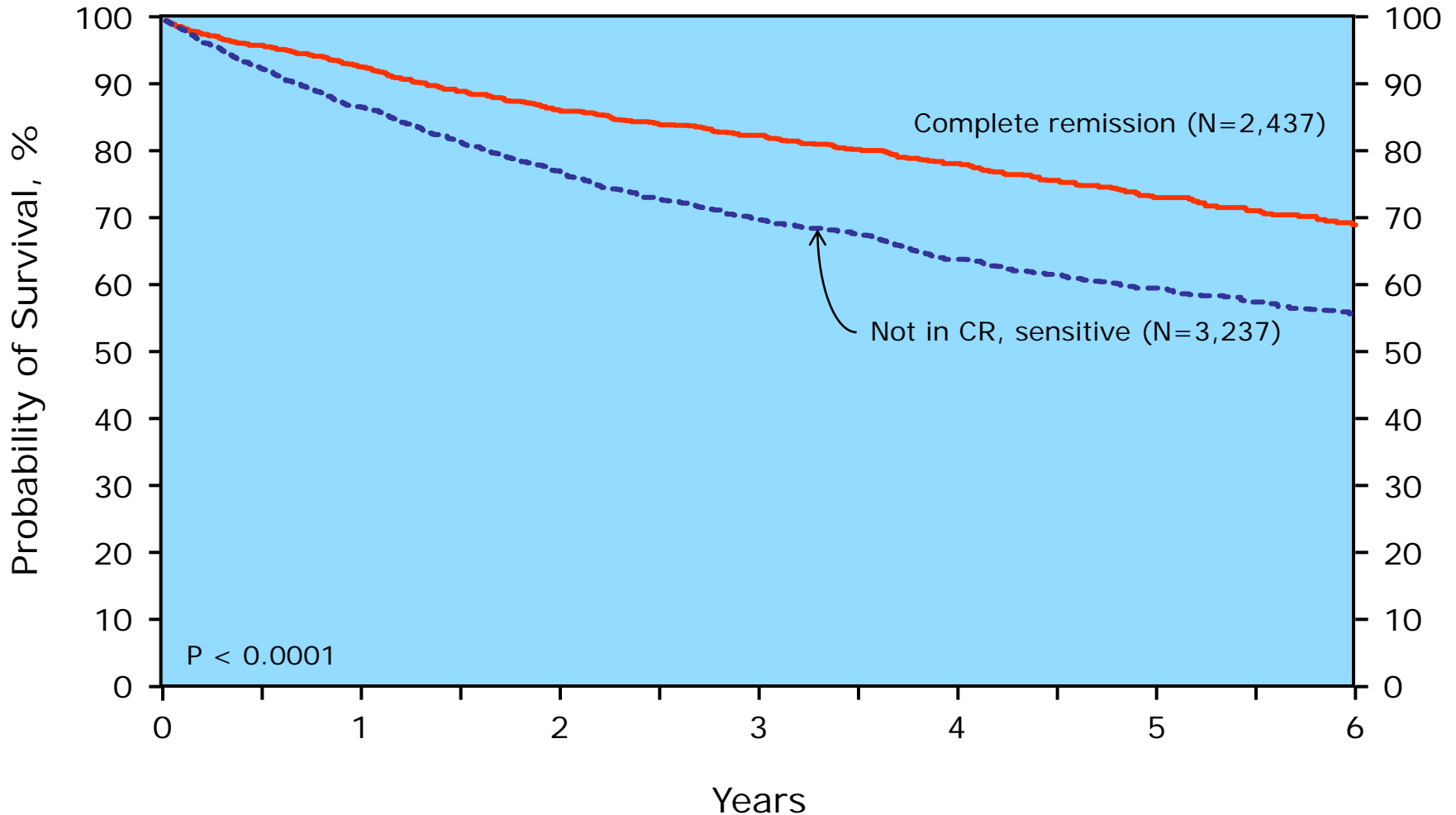


# Probability of survival for severe aplastic anemia allogeneic transplant for, by donor type and age, 1998-2008

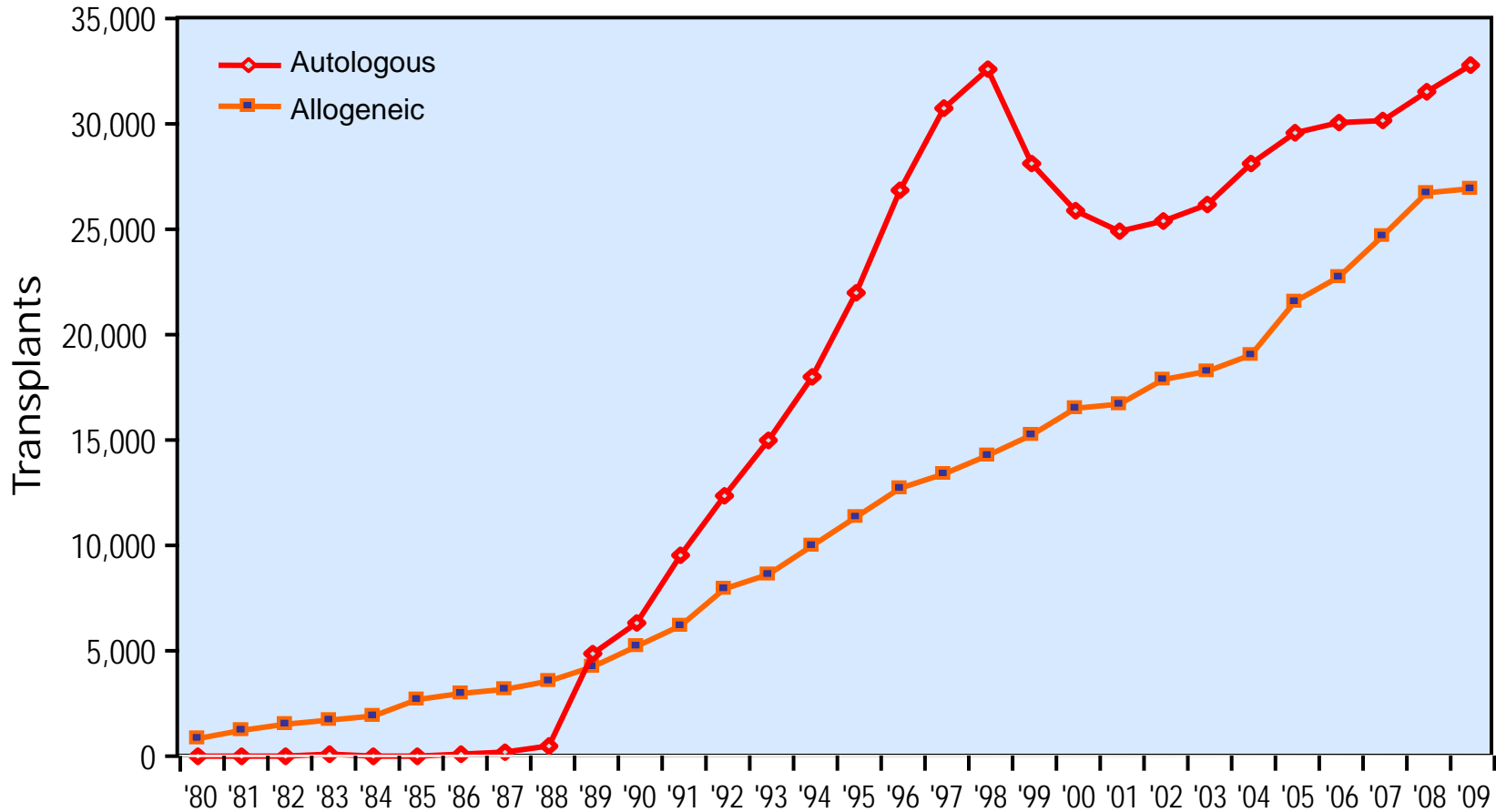


# Probability of survival for Hodgkin disease

autologous transplant , by disease status, 1998-2008

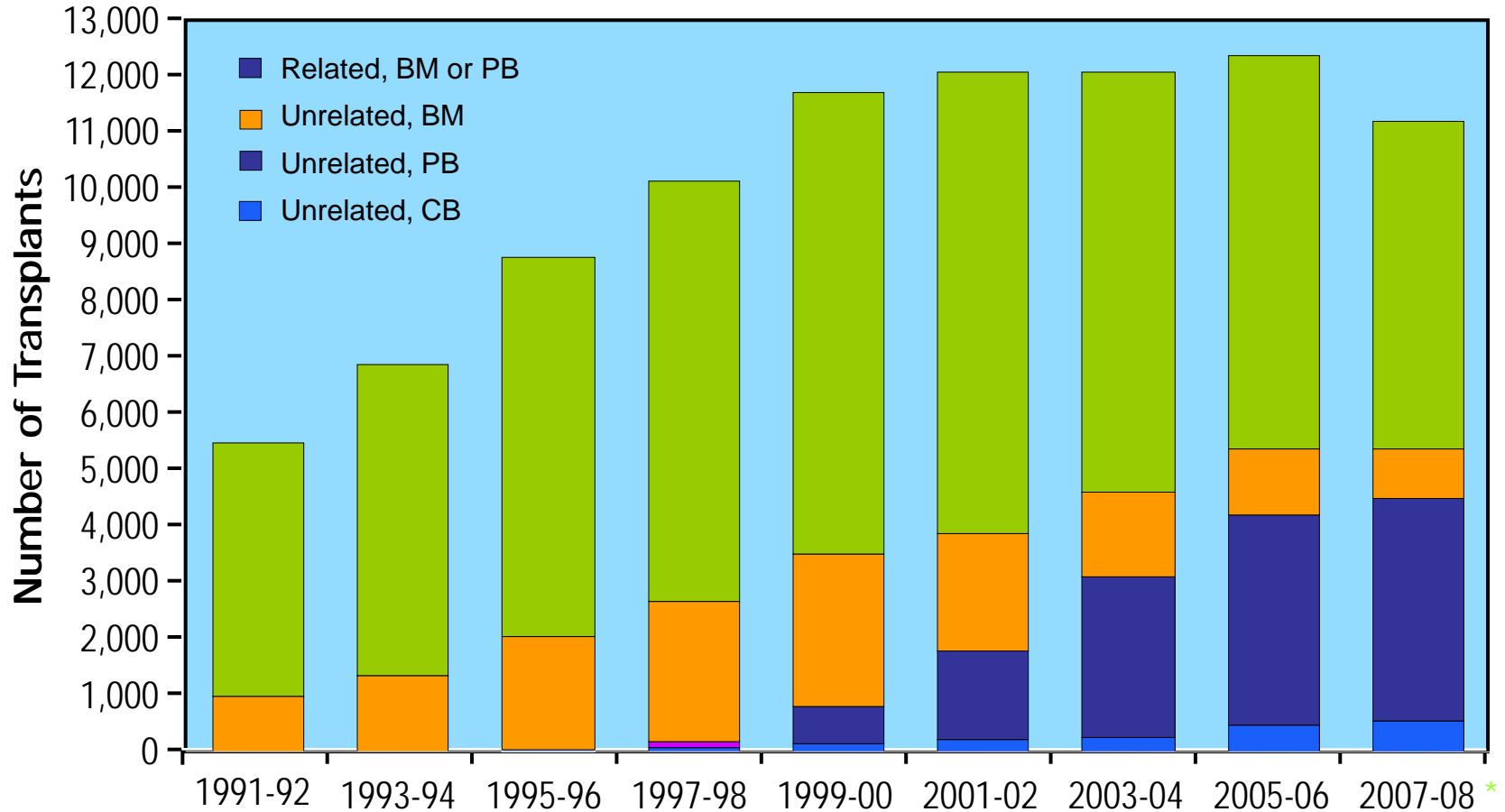


# Transplant Activity Worldwide 1980-2009



# Allogeneic transplant donor type

in patients >20 years, by and graft source, registered with CIBMTR, 1991-2008



\* Data incomplete

# European Transplant Activity 2010

## HSCT - rates in Europe 2010

Total transplants (all)

per 10 million

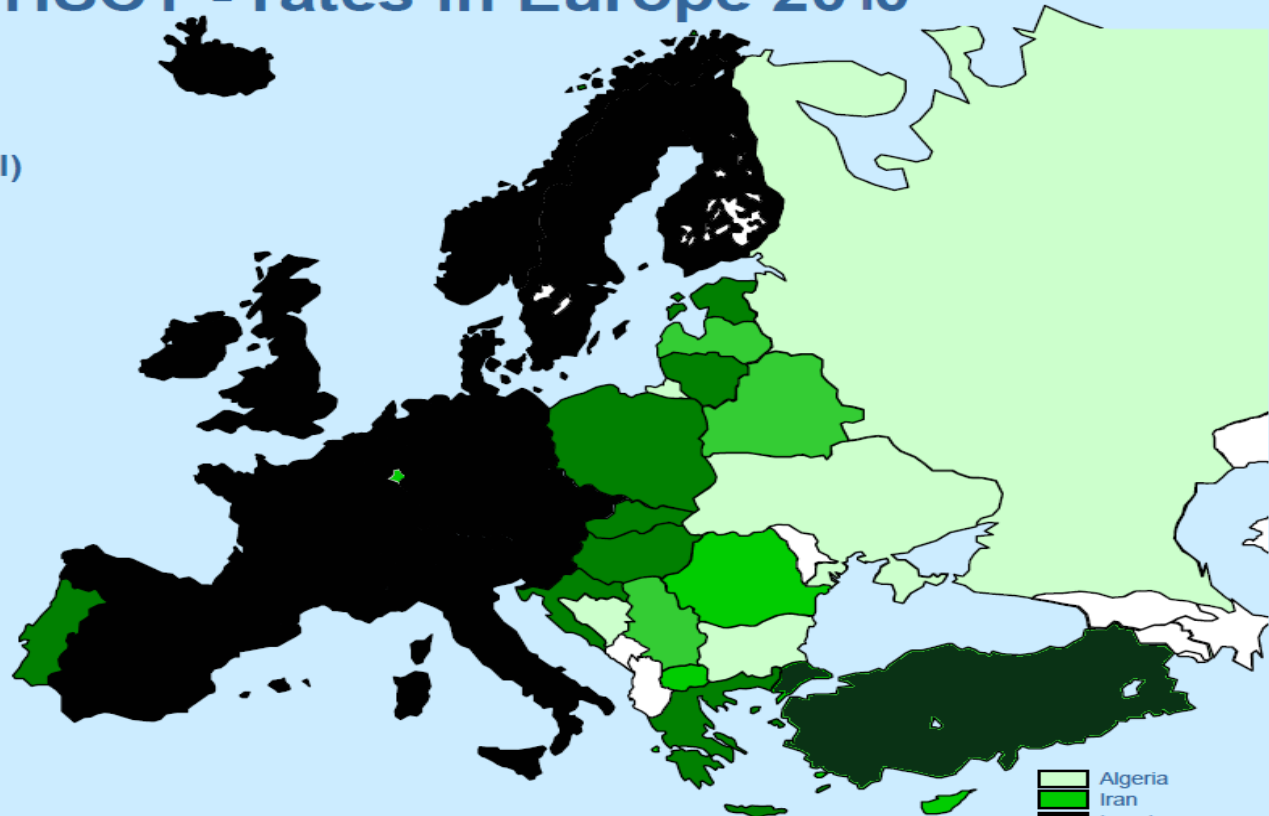
0 or no report

1 - 50

51 - 200

201 - 400

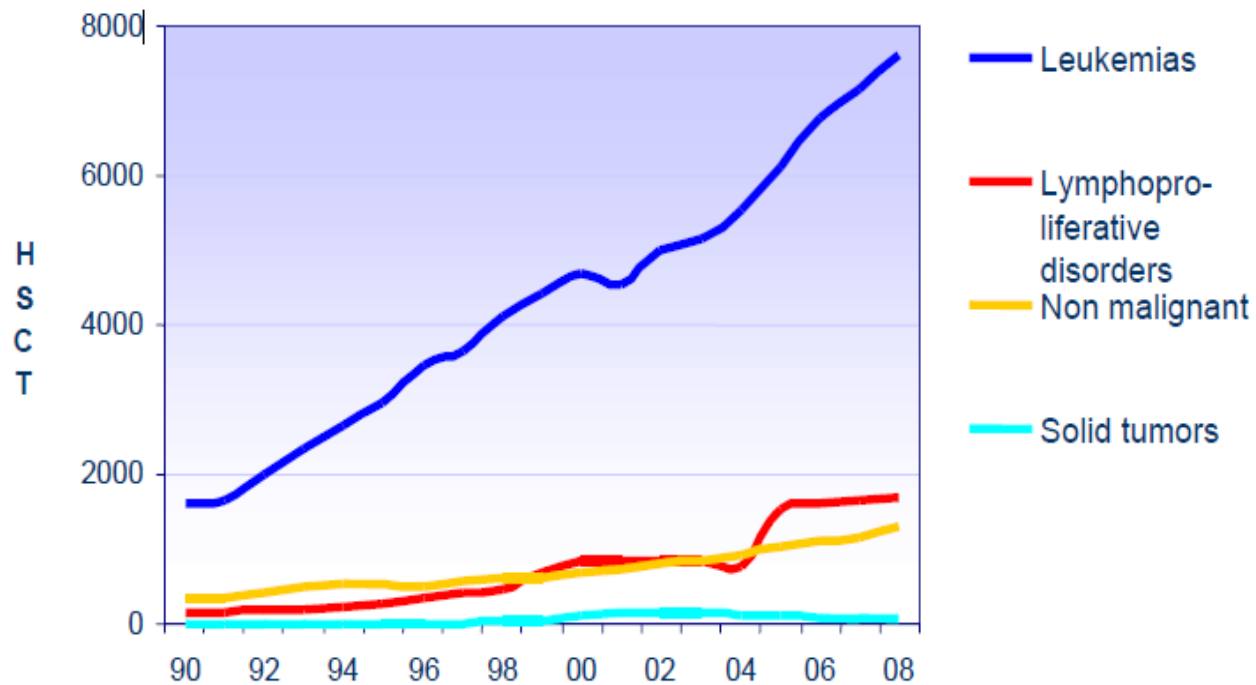
> 400



- Algeria
- Iran
- Israel
- Lebanon
- Saudi Arabia
- South Africa
- Tunisia
- Jordan



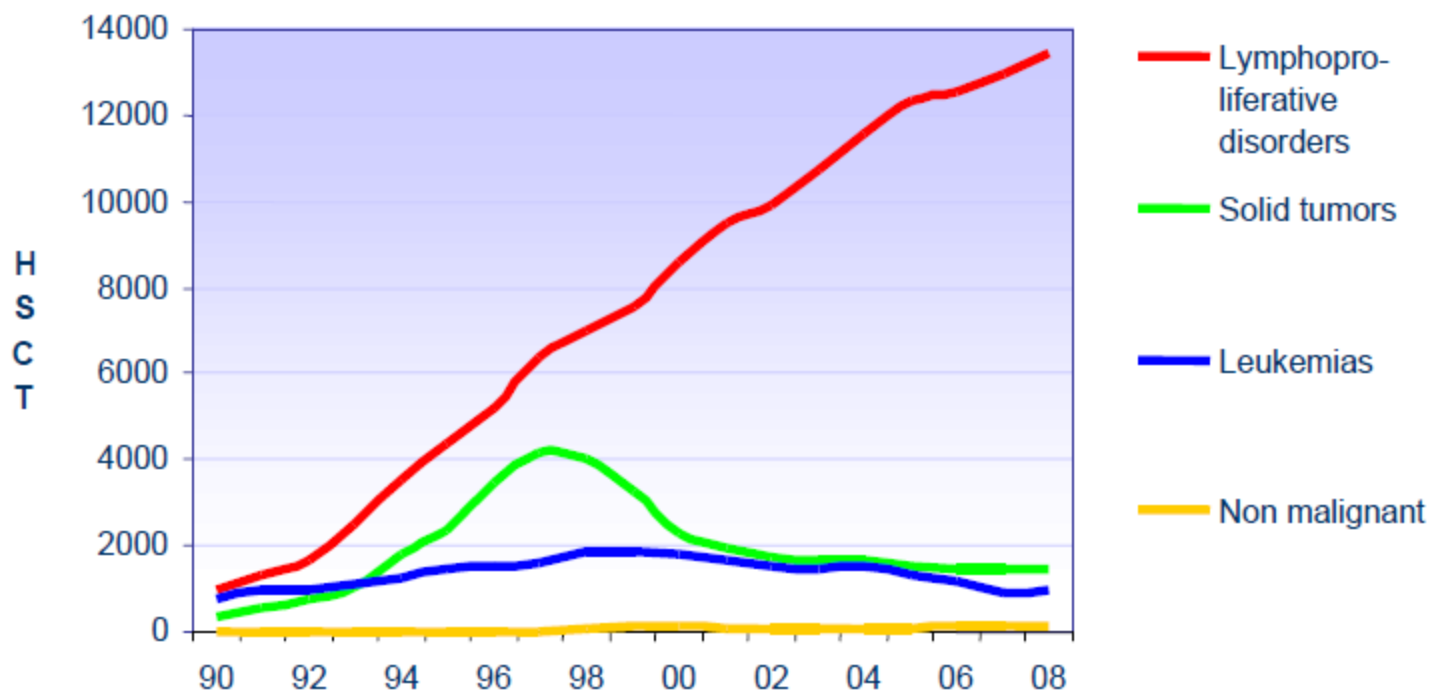
## EBMT Activity Survey on HSCT 1990-2008: allogeneic



2008: final data

*The European Group for Blood and Marrow Transplantation*

## EBMT Activity Survey on HSCT 1990-2008: autologous



2008: final data

*The European Group for Blood and Marrow Transplantation*



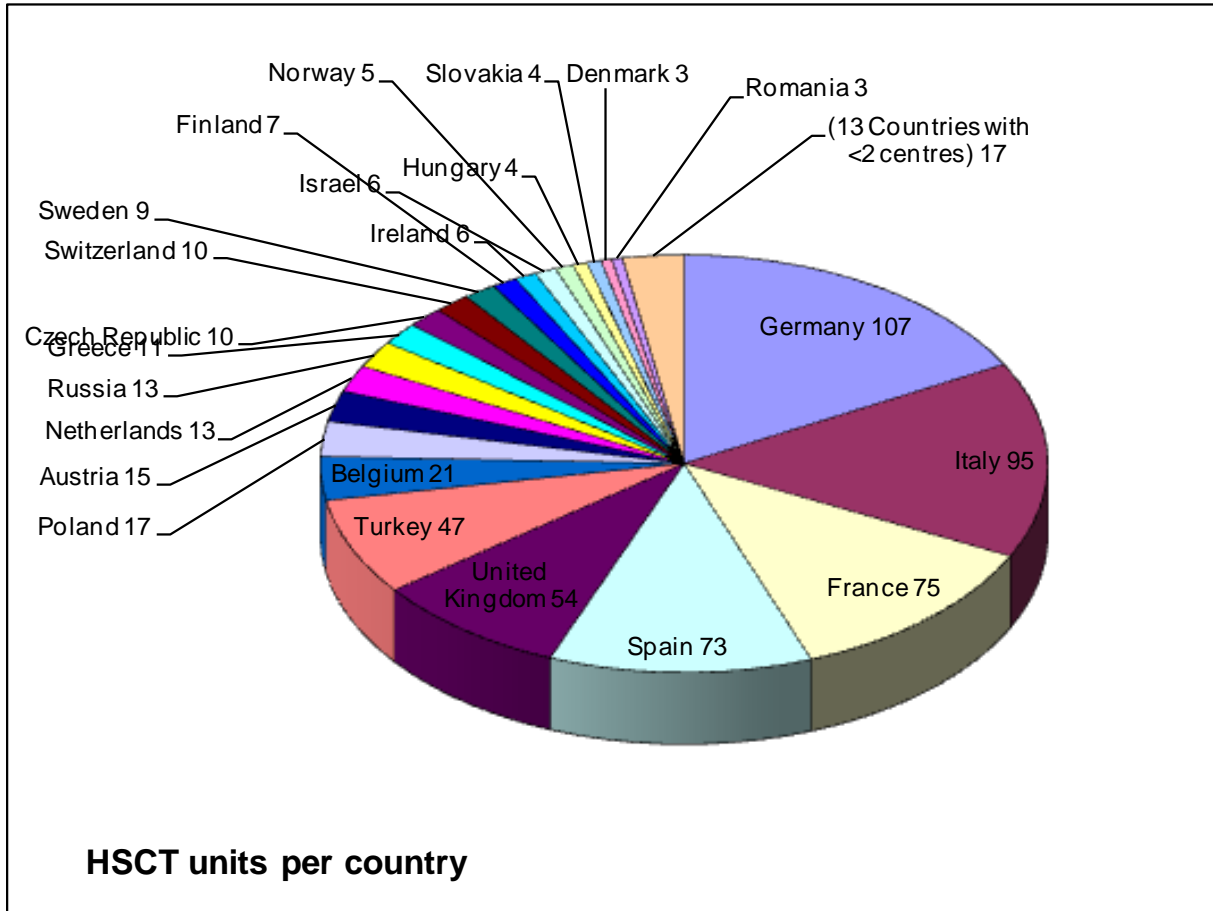
## EBMT Activity survey on HSCT in 2008: main indications

| Indication                       | Allogeneic<br>1st Tx. | Autologous<br>1 <sup>st</sup> Tx. | Total        |
|----------------------------------|-----------------------|-----------------------------------|--------------|
| Leukaemias*                      | 7632                  | 978                               | 8610         |
| Lymphoproliferative<br>disorders | 1699                  | 13428                             | 15127        |
| Bone marrow failures             | 615                   | 2                                 | 617          |
| Solid tumours                    | 62                    | 1424                              | 1486         |
| Non-malignant disorders          | 699                   | 172                               | 869          |
| Others                           | 75                    | 26                                | 101          |
| <b>Total</b>                     | <b>10782</b>          | <b>16028</b>                      | <b>26810</b> |

\* includes CLL

2008: final data

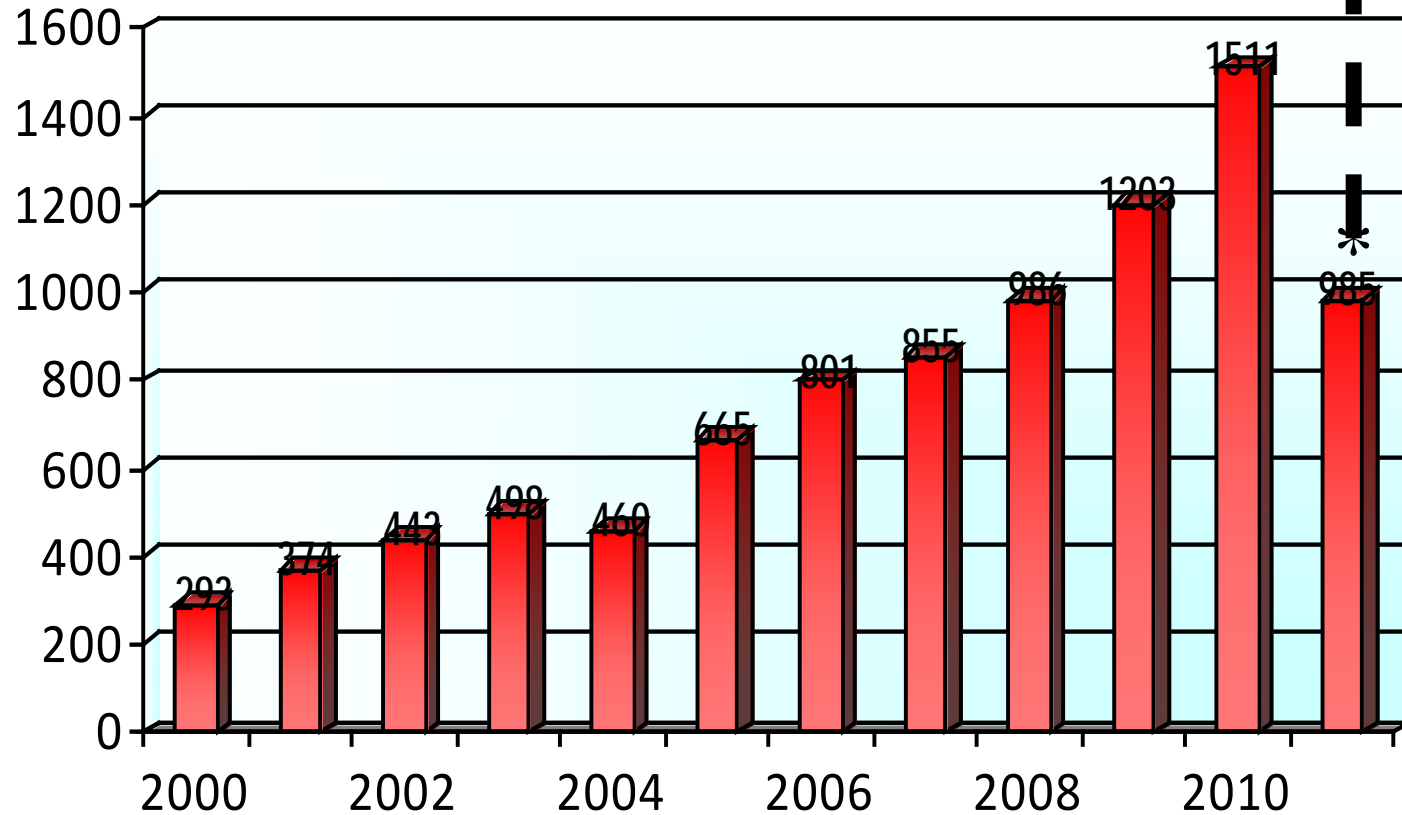
# Activity survey centers 2010



| COUNTRY                        | Activity Survey |
|--------------------------------|-----------------|
| Germany                        | 107             |
| Italy                          | 95              |
| France                         | 75              |
| Spain                          | 73              |
| United Kingdom                 | 54              |
| <b>Turkey</b>                  | <b>47</b>       |
| Belgium                        | 21              |
| Poland                         | 17              |
| Austria                        | 15              |
| Netherlands                    | 13              |
| Russia                         | 13              |
| Greece                         | 11              |
| Czech Republic                 | 10              |
| Switzerland                    | 10              |
| Sweden                         | 9               |
| Finland                        | 7               |
| Ireland                        | 6               |
| Israel                         | 6               |
| Norway                         | 5               |
| Hungary                        | 4               |
| Slovakia                       | 4               |
| Denmark                        | 3               |
| Romania                        | 3               |
| (13 Countries with <2 centres) | 17              |
|                                | 625             |

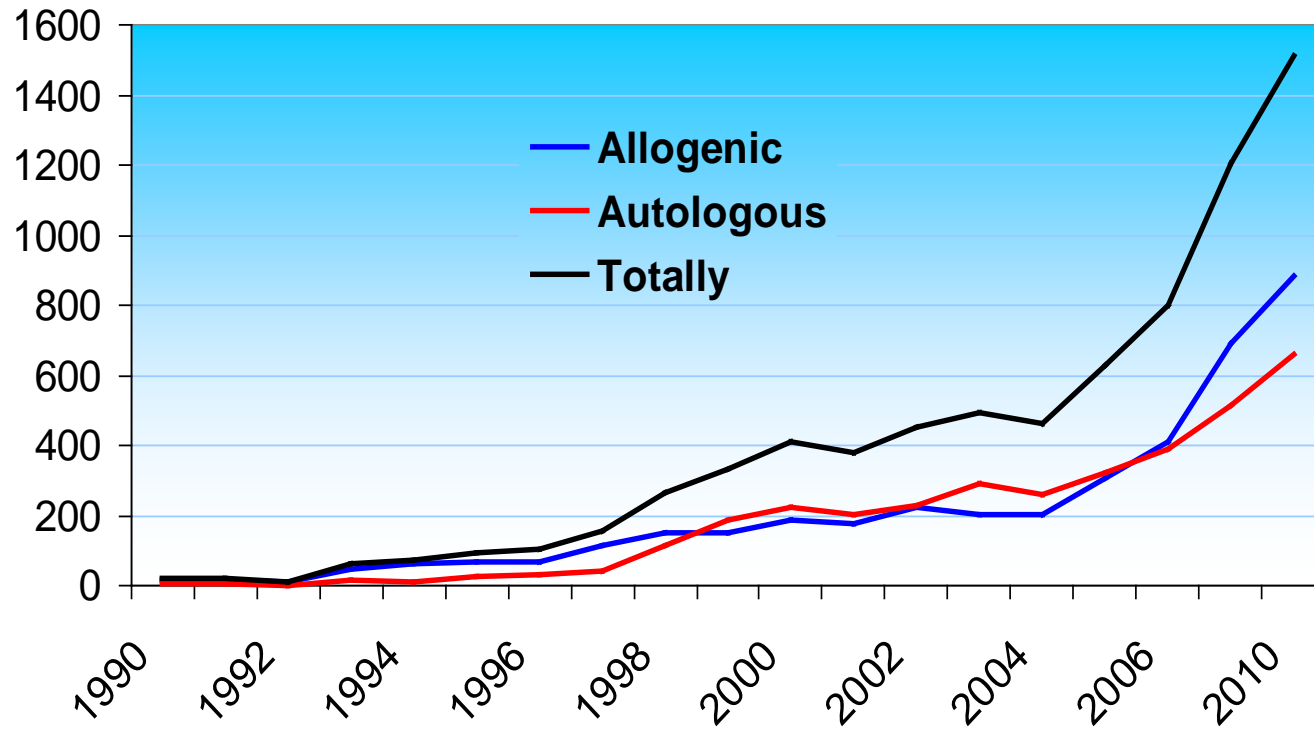
# Hematopoietic Stem Cell Transplantation Activity survey of Turkish Center

2000



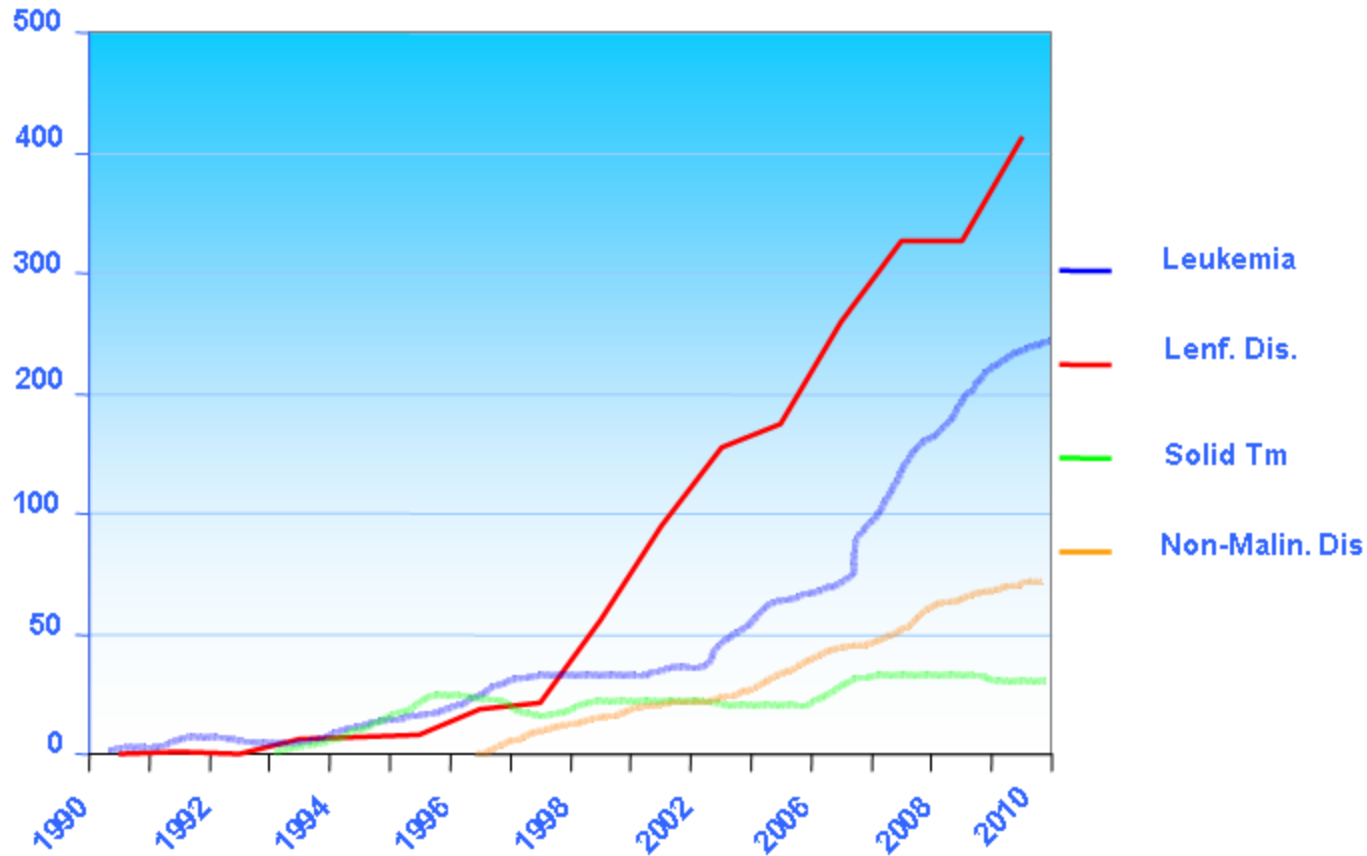
\* Sixt month (incomplet data)

# TTR (Turkish Transplant Registry) Hematopoietic Stem Cell Activity Survey



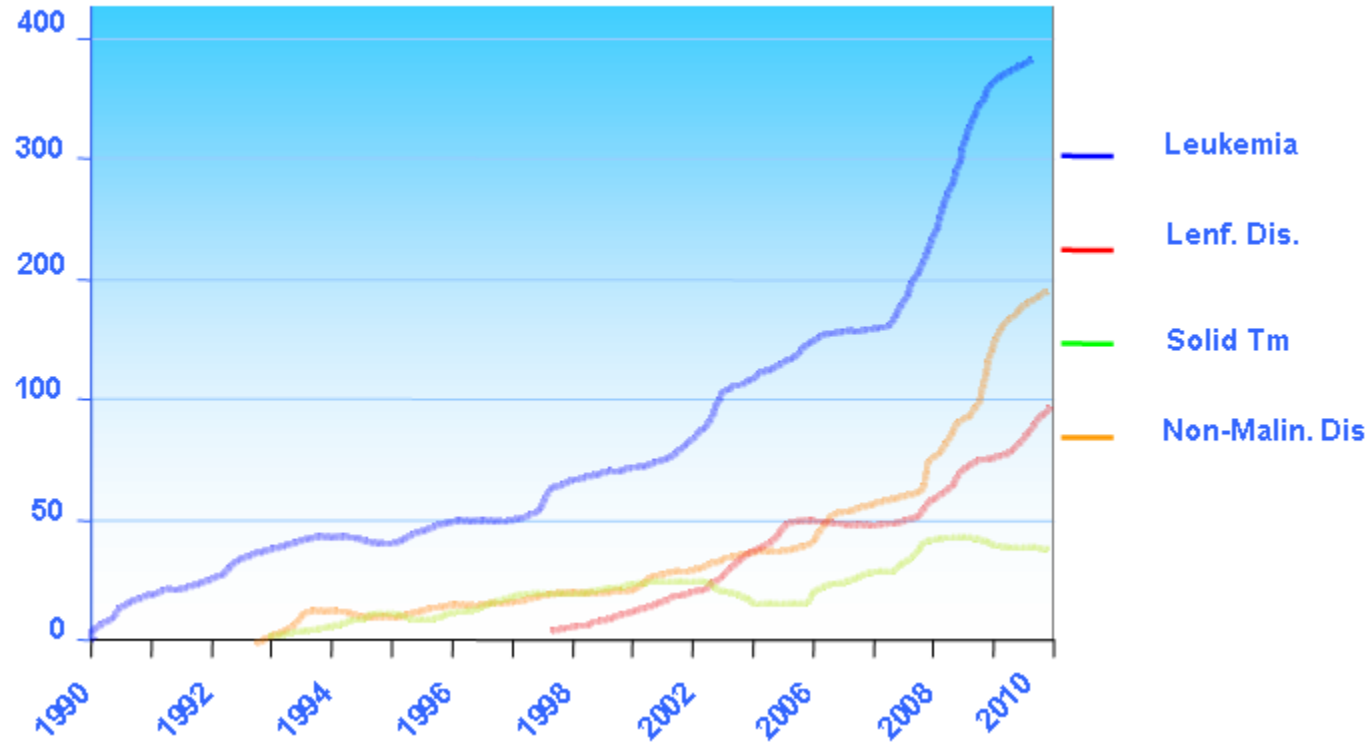
# TTR (Turkish Transplant Registry)

## Autologous Hematopoietic Stem Cell Activity Survey



# TTR (Turkish Transplant Registry)

## Allogeneic Hematopoietic Stem Cell Activity Survey

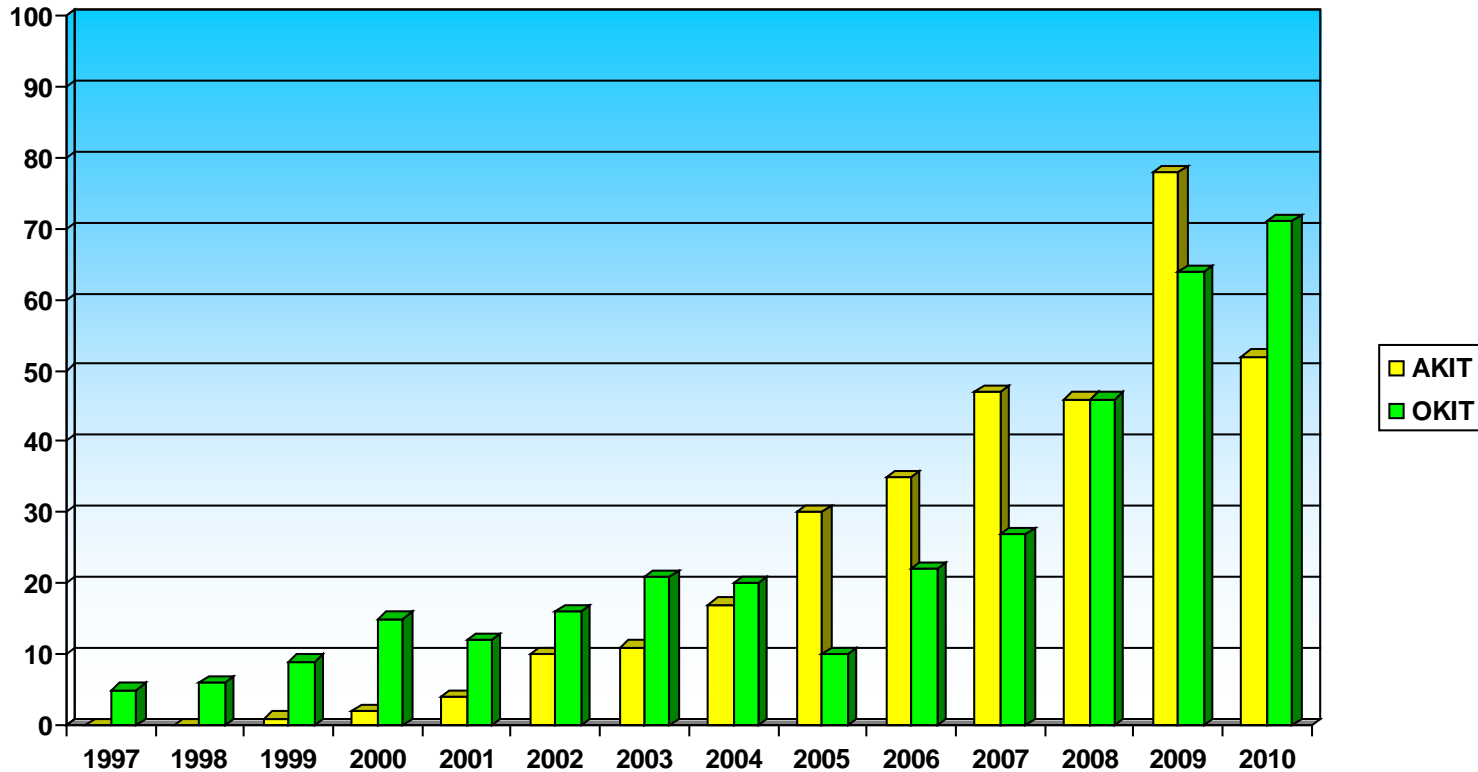




# Erciyes University

Cappodocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

## Hematopoietic Stem Cell Transplantation Activity Survey

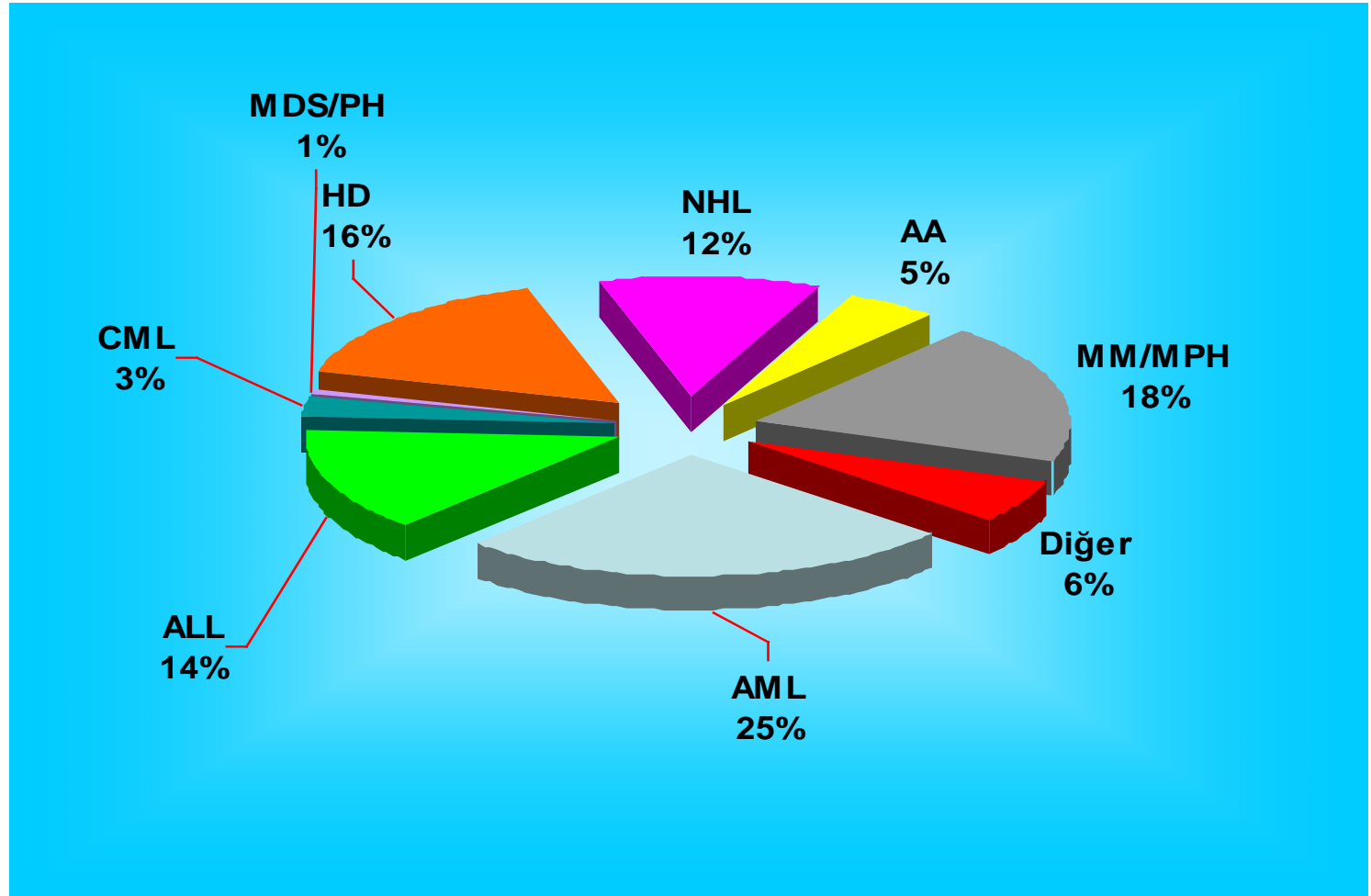




# Erciyes University

Cappadocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

## Hematopoietic Stem Cell Transplantation Activity Survey





# Erciyes University

Cappadoccia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

**Hematopoetic Stem cell Transplatation Activity Survey**



# Erciyes University

Cappodocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)



**Thank you for  
your attention**

**Teşekkürler**

